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SYMPOSIUM ON INFECTIONS OF THE RESPIRATORY TRACT

OBSERVATIONS ON THE EPIDEMIOLOGY OF THE COMMON COLD*

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THE common cold is a paradox. It is so common — or rather so prevalent — that no one is interested in it. We are all familiar with the statistics which indicate that colds cause more loss of time from business than do all other illnesses combined. This is true. They do cause loss of time from work, no doubt, but no serious loss of time, I suspect, from more pleasurable pursuits.

The disease is so exasperating: it never kills and seldom causes serious illness, but it refuses to submit to any known therapeutic or preventive measures. It is not a disease at all. It is a group of diseases, masking themselves under a homogeneous assembly of similar clinical symptoms, with a pretense of being a single clinical entity, but in reality being of widely diversified etiology.

We are accustomed to the statement that a cold is an acute inflammation of the upper respiratory tract. But almost all the communicable diseases of childhood are initiated by symptoms of an acute infection of the upper respiratory tract. Measles, scarlet fever, whooping cough, tonsillitis, diphtheria — all in their initial stages resemble an upper-respiratory infection.

The sinus infections are often confused with colds. One frequently hears the statement, "I caught cold in the fall, and it lasted off and on all winter." The patient really has had recrudescences of chronic sinusitis from time to time. The common opinion that a cold is due to exposure results from the fact that a person with sinusitis may have the infection under control, but following exposure to cold, chilling of the body surface, fatigue or other factors the sinus infection reasserts itself, and the patient complains of a "fresh" cold.

Persons with unknown susceptibility to certain proteins often develop symptoms of the upper respiratory tract, and complain about the prevalence of colds. Mechanical irritations of all sorts, which affect the mucous membranes of the nose and throat, produce what to the patient are symptoms of an early infection; but by appropriate home remedies he manages to "break up" his cold in twenty-four hours. All these various conditions are grouped in one diagnosis — a common cold.

One disease entity may be singled out of this group of ills, namely, the acute self-limited epidemic infection of the upper respiratory tract. This infection is due to a filterable virus. It is transmitted readily, and by fairly direct contact, from person to person. Wells[1] has shown that the zone of transmission is not simply the distance of spread of the direct spray of the sneeze or cough of the infected person, but the infecting agent may actually spread in a radiating zone for a considerable distance, particularly within the confines of a building, such as a schoolroom or a theater.

The incubation period is short — twenty-four to thirty-six hours. The infected individual communicates his infection to others for a short period only — during the early stages. Three or four days after the beginning of symptoms he is noninfectious, although he may continue with sore throat and cough for a long time. The most infectious period is the initial day, and a patient may even infect others from four to six hours

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before he is aware that he is coming down with a cold.

The carrier state, common in so many infections, is believed to be quite rare. We do not know with certainty how frequently it occurs, but all evidence indicates that carriers of the virus of colds or of influenza are rarely if ever encountered.

The degree of contagiousness is high. Practically all susceptible persons who are exposed to immediate contact with an infected person develop the disease. The immunity that is produced from an attack of this disease is specific, but may be of relatively short duration. Individual resistance varies considerably, tending to increase with age. It is quite certain that attacks are much less frequent in the older age groups. There is a great variation in susceptibility among the members of a single family or in a closed community, as a boarding school or an orphanage.

Francis[2] has shown, in his studies of influenza, that individual immunity may be due to protective bodies, which are found in the nasal secretions. These secretions are not destructive to bacteria, but may have a high power of neutralization of the influenza virus. There is a great deal of variation in the destructive power of these secretions. The question arises as to whether the potent factor is a nonspecific enzyme, or whether the protective bodies in these secretions are specific and bear the same relative immune power as does the blood serum or other body tissues.

The only experimental animal that has been employed successfully in the study of colds is the chimpanzee. Thus, all experimentation becomes complex and very expensive. The influenza virus, on the other hand, is transmissible to ferrets and young white mice.

I have included influenza in my discussion of the common cold. The reason is that, clinically, the acute epidemic respiratory infections themselves are not a single entity, but a group of diseases which show wide variation in symptomatology and in degree of severity. Even in an epidemic of known single etiology, all gradations of clinical symptoms may be encountered. For example, I[3] have studied the epidemiology of a severe infection of the upper respiratory tract at Northwest River, Labrador. The colony of 167 persons was cut off from all communication with the outside world by ice and snow. A dog-team driver went to Rigolette, eighty miles away, for the Christmas mail. There he found an epidemic of severe respiratory infection raging. Without delay he loaded his sled and returned home. Twenty-four hours later, while still half a day's journey from home, he became very ill but strapped himself on the sled and the dogs took him home. This infectious agent, brought in by a single individual, produced in this small village an epidemic of disease. The striking feature of the epidemic was that all variations and gradations in symptoms occurred in the patients — from a simple mild ambulatory cold to a severe debilitating influenza with post-influenzal pneumonia, and even death.

Horsfall, Hahn, and Rickard,[4] in a recent study of four epidemics of mild influenza, conclude that the certain diagnosis of epidemic influenza cannot be made on either clinical or epidemiologic grounds. Neither can it be made from serologic tests. Infected individuals developed specific antibodies, it is true, but some exposed persons remain symptom-free, yet develop specific antibodies equal to those shown by the frank cases.

Martin and Fairbrother[5] recently described an epidemic of apparent influenza that occurred in 1939 in England. It was a uniform disease occurring in a closed community. Clinically it resembled influenza, except for lack of severity and limited dispersion. Ferrets were infected on first passage, but the virus died out on second passage. It was too mild a disease to be called influenza, too severe to be called a common cold.

Magill and Francis,[6] in a study of twenty-four strains of influenza virus, have shown that there is a marked variation in antigenic characteristics of the different strains. Some strains from a single epidemic closely resemble one another, but strains from different epidemics show great variation. These authors suggest that the structure of the virus of epidemic influenza is a mosaic of antigens, and that each strain does not contain all, or even a major part, of the antigenic components of other strains.

Do these findings not suggest that all the acute epidemic infections of the upper respiratory tract, from the mildest to the severe pandemic infections, are due to a closely related group of infectious agents which have wide gradations in virulence, and which produce a chain of symptoms varying in degree and kind from the very mild to the very severe — from an ambulatory cold to a fatal influenza? In any given outbreak the virulence will be fairly constant, but even when the virus is known to be exactly the same, as, for example, in the Labrador epidemic and also in the epidemic described by Martin and Fairbrother, different individuals within a single community or even a single family will vary widely in their reactions to the infection.

There does not seem to be much hope of developing an effective specific vaccine against the

milder common colds. It seems probable, on the other hand, that a method may be devised whereby an individual may be immunized against the virulent specific prevailing epidemic influenza virus — if it can be isolated, sent ahead of the epidemic and administered just before the arrival of the infection in the community. But immunization against seasonal colds is another matter. One can hardly expect the physician to do more than Nature herself in producing an immunity to this type of infection. Nature does not produce more than temporary immunity through the actual attack of a cold. Thus, we cannot expect that specific preventive measures could produce more lasting immunity than does an actual attack of the disease itself.

We must admit that there is no known way of preventing epidemics of colds in the active life of a modern civilization. In so far as this infection itself is concerned, it is of little importance whether we do or do not prevent the ordinary mild cold. Unfortunately, however, the acute cold is frequently followed by serious consequences. The important features of the cold are its sequelae. The cold itself is a self-limited disease of four or five days' duration. In itself, it does little or no harm. But the virus may cause an injury to the mucous membranes of such degree as to permit secondary invaders to produce serious trouble. Apparently the consequences are dependent on the type of secondary invader that prevails in the nasopharynx at the moment. The commonest offender is the pneumococcus. The more virulent the type, the greater may be the degree of invasion and injury.

Recently I have taken serial nasopharyngeal cultures in an orphans' home. Pneumococcus Type 14 appeared and spread through the nursery until practically every child was a carrier of the strain. There were no ill effects, although Type 14 is notoriously a frequent cause of pneumonia in children. An epidemic of colds then invaded the nursery. Promptly the Type 14 pneumococcus increased in prevalence in the throats of the children. Furthermore, the inflammation extended from the posterior nasopharynx to the middle ear in several of the group, and two children developed pneumonia. In every case the Type 14 pneumococcus was isolated from the discharges of the ears and from the sputum of the children with pneumonia.

The prevailing organism that may be quiescent and then suddenly cause serious trouble, following an acute cold, is not always a pneumococcus. For example, a patient had a troublesome acute sinus infection. A beta hemolytic streptococcus was isolated in almost pure culture from the discharges. A month's vacation in a warm, dry climate resulted in quiescence, although cultures showed that the same organism was still present in the sinus discharges in small numbers. On the day of return from the tropics, the patient was exposed to a person who was in the first stages of a cold. The hour and moment of first exposure were known. An acute cold developed promptly, and was followed in three days by a recrudescence of the sinus infection. Culture of the discharges showed enormous numbers of beta hemolytic streptococci. The individual from whom the cold was acquired did not harbor a beta hemolytic streptococcus, but was a carrier of Type 8 pneumococcus. He also developed a sinusitis, but the invading organism in his case was Type 8 pneumococcus.

If the secondary invaders are the important factors in production of the severe sequelae of acute respiratory infections, can nothing be done to increase the immunity of an individual to these organisms and prevent the severity of the effects?

Cold vaccines have not been wholly successful in the past for two reasons. In the first place, they do not build immunity against the invasion of the initial virus; in the second place, they do not always increase the resistance of the individual to the specific secondary organism to which he may be exposed.

Theoretically, at least, it would seem to be quite possible to prepare a cold vaccine from the organisms which are most prevalent in the nasopharynges of the community, and to which the individual is most likely to be exposed. Immunization with this vaccine should give some degree of protection against the prevailing and most troublesome factors which produce the more serious consequences of the common cold.

Summary

The common cold is an epidemic virus infection of the upper respiratory tract. It is frequently confused with other clinical conditions. It is so closely related to influenza that no clear-cut clinical differentiation is possible at the present time. The disease is self-limited, is of four or five days' duration and, of itself, is of little consequence.

The importance of the infection depends on the fact that the virus prepares the mucous membranes of the upper respiratory tract for invasion with a wide variety of organisms with which we are quite familiar, and concerning which some preventive measures may be taken.

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THE RELATION OF SINUSITIS TO CHRONIC NONTUBERCULOUS CHEST INFECTION*

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THE purpose of this paper is to present the results of a study of the relation of sinusitis to bronchiectasis. During the last four years I have examined 150 cases of bronchiectasis at the Pulmonary Clinic of the Massachusetts General Hospital to determine the incidence of sinus infection, and to throw light, if possible, on the relation of sinusitis to the infection in the chest.

In a previous paper I[1] set forth the statistical features of this association of sinusitis with bronchiectasis. They are as follows:

(1) The patients were for the most part adults or adolescents at the time of examination.

(2) One third of the patients developed bronchiectasis in the first decade of life, and two thirds developed it before the age of twenty. The remaining cases were scattered throughout the third, fourth, fifth and sixth decades.

(3) The two commonest diseases which preceded the bronchiectasis were upper-respiratory infection (43 per cent) and pneumonia (29 per cent). The remainder were such conditions as influenza, whooping cough, asthma, tonsil and adenoid operations, and the presence of foreign bodies.

(4) Patients who developed bronchiectasis before the age of ten had had pneumonia more frequently than any of the other diseases. Most cases which developed after the age of ten gave a history of a previous upper-respiratory infection.

(5) Most of the male patients had had a preceding upper-respiratory infection more frequently at onset, while most of the female patients attributed their bronchiectasis to pneumonia, influenza or whooping cough.

(6) There was a very high incidence of sinusitis. Even among those who claimed not to have had an upper-respiratory disease at or preceding the onset, x-ray studies demonstrated an incidence of chronic sinusitis of 55 per cent; for the group as a whole the incidence was 62 per cent. The sinusitis varied in severity from an extremely slight thickening of the lining of the sinus involved, through all degrees up to a marked pansinusitis with chronically thickened mucous membrane, retained purulent secretion and, sometimes, reaction in the surrounding bone. In addition, 24 per cent of the others gave clinical evidence of recurrent acute sinusitis, so that the patients who suffered from more or less sinusitis totaled 86 per cent. The sinuses most frequently involved were the antrums and the ethmoids.

(7) Cases of bronchiectasis in which only one lobe was affected had a lower incidence of sinusitis than did those in which more than one were affected. Cases in which the left lower lobe alone was involved had an incidence of 45 per cent. For both left lobes the incidence was 60 per cent; for both lower lobes, 67 per cent; for the left lower and right middle lobes, 73 per cent; and for panbronchiectasis, 75 per cent. These facts are, of course, of great importance in evaluating the role of sinusitis in cases where thoracic surgery is considered.

In summary of the above points there seem to be several different diseases that occur at the onset of bronchiectasis. There is a very high incidence of sinusitis in these cases in later life. Even those cases that give an etiology of essentially pulmonary infection at the onset have a later sinusitis incidence of 55 per cent. Practically all show a marked susceptibility to respiratory infection. There may be factors in childhood differing from those existing in later life, and there may be certain predispositions in the sexes which make

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men more susceptible to one etiologic factor and women to another.

Because of the frequency with which sinusitis is found in cases of chronic cough, it has been thought by many observers that there is a direct relation, a mechanism, as it were, whereby the infection in the sinus causes that in the chest. This has been described as an absorption of toxins into the lymphatic system or blood stream, eventually affecting the lungs. There is also the question of direct inhalation into the lungs of septic postnasal discharge.

It is quite possible that at the time when a patient develops bronchiectasis there may be a severe head cold or a sinusitis in addition to a pulmonary infection, such as pneumonia. On the other hand, there are many patients with sinusitis who never develop any bronchial infection. In the latter the disease is purely local. But it is true that many patients with sinusitis suffer also from a cough and a great deal of postnasal discharge. The cough has been emphasized as an important cause of bronchial dilatation. It is also possible that infected secretion may find its way into a bronchus and thereby cause a foreign-body obstruction with collapse of the lobe. There is still another situation which may occur. At the onset, the patient may have an infection of the entire respiratory tract. Because of the severity of the chest infection, the upper-respiratory features may be overlooked. The upper-respiratory infection, indeed, may soon clear up although the pulmonary damage persists. But as these patients suffer from more than the usual number of head colds, the opportunity for reinfection of the sinuses is very great and eventually a condition of chronic sinusitis may develop.

Each case presents its own problem in regard to treatment. After making a diagnosis of sinusitis, it is necessary to determine whether it is a major factor in the picture or whether it is of minor importance. This is naturally true of all cases of sinusitis, and the criteria hold true even in cases uncomplicated by bronchiectasis. There are all degrees of sinusitis. The proper treatment of an acute sinusitis, as is well known, is quite different from that of a chronic sinusitis. In the acute type one must be extremely conservative, unless one is faced with serious complications, such as intracranial infection, osteomyelitis or orbital abscess. In the chronic cases there is quite a different problem. In the very mild cases no operation may be needed, or if the patient is subject to repeated attacks of sinusitis and these infections are complicated by local conditions in the nose, such as a deviated septum, it may suffice to correct this obstruction. In children, the removal of tonsils and adenoids, the aspiration of nasal secretion and attention to the medical problems of hygiene have to be considered. It is in the more severe chronic infections in adults that radical operations may be necessary.

From the present series of 150 cases of bronchiectasis, 76 have been chosen to illustrate some of these points. These have been subdivided into four groups as follows: a control group of 21 cases in which the sinuses were negative but which received lobectomy; 14 cases of lobectomy in which the sinuses had not been operated on; 11 cases with both lobectomy and sinus surgery; and 30 cases in which the pulmonary disease was unsuitable for lobectomy or in which lobectomy, although indicated, had not yet been performed, and in which the sinuses were operated on (Table 1).

Table 1. *End Results in 150 Cases of Bronchiectasis.*

Treatment	No. of Cases	Degree of Improvement				
		Symptom-free	Marked	Moderate	Slight	None
Lobectomy (sinuses negative)	21	8	8	5	0	0
Lobectomy (sinusitis — no surgery)	14	0	10	0	0	4
Lobectomy and sinus surgery	11	0	7	2	2	0
Sinus surgery	30	3	13	0	4	10
Totals	76	11	38	7	6	14

In the first group, where lobectomy was performed but the sinuses were negative, the results were the best. Out of 21 cases, 8 are now symptom-free, 8 have only a slight amount of sputum, and 5 have a moderate amount of sputum but have been improved. This group is also less subject to upper-respiratory infection.

In the second group, that of lobectomy and unoperated sinusitis, 10 of the 14 patients have been markedly improved in regard to the amount of sputum. Three of these 10 patients still have a moderate degree of sinusitis; although they are still subject to many head colds and to nasal discharge, their chests are negative. What sputum they have may well come postnasally from the sinuses. The remaining 4 patients have the same amount of sputum as before operation and a moderate to marked degree of sinusitis, and would seem to be candidates for sinus surgery.

In the third group, in which lobectomy and sinus surgery have both been performed, none of the 11 patients are absolutely symptom-free so far as the chest is concerned. Seven, however, have only a slight amount of sputum, and 2, although still raising sputum, have shown a considerable improvement in the amount. In 2 cases there has been no change so far as the chest is concerned, but the nose and sinus condition has been improved. It is interesting that some of these patients had sinus surgery before their lobectomy. Although their nasal symptoms were much improved, no marked change occurred in the chest until after the lobectomy. It would seem that in this group the bronchiectasis must be considered as simply another locus of infection or, as Dr. E. D. Churchill says, "another sinus."

In the fourth group, that of sinus surgery only, 3 of the 30 patients became symptom-free for two or three years after the operation. They were adults and their cases had been diagnosed as early bronchiectasis; they had a minimum number of chest symptoms before the operation. Thirteen patients showed considerable improvement in the amount of sputum, 4 were slightly improved and the rest were unchanged.

Summary

Sinusitis is a common accompaniment of bronchiectasis.

It may be present at the onset of the chest infection, or may appear, or at least be recognized, later when it is a vital factor in the patient's disability.

Cases of bronchiectasis suitable for lobectomy but uncomplicated by sinusitis show the best end results.

Patients with sinusitis may have considerable sputum from the upper respiratory tract even after the chest has been operated on.

Patients unsuitable for lobectomy have been improved locally, and in some cases where the bronchiectasis is mild the chest symptoms also have been lessened. It is not suggested that sinus surgery will be followed by an eradication of the bronchiectatic cavity: it is not an alternative to lobectomy when the latter is advisable.

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PATHOGENESIS OF PRIMARY AND REINFECTION TYPES OF PULMONARY TUBERCULOSIS*

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TUBERCULOSIS resulting directly from first infection with tubercle bacilli, and tuberculosis as it commonly occurs years after a first infection has taken place and healed, are so different that a classification of the disease taking into account the variation in origin, development and character in these two types is necessary.

The two forms have been defined with great care in *Diagnostic Standards,* a manual published by the National Tuberculosis Association that summarizes the classification of tuberculosis and certain technical procedures used in its detection. In early editions the terms "childhood-type tuberculosis" and "adult-type tuberculosis" were used, but in a later one, presenting a classification designated as tentative, these terms were abandoned in favor of the more specific labels "primary tuberculosis" and "reinfection tuberculosis." This change was logical because with the passage of years and the diminishing incidence of tuberculosis, tuberculous infection is becoming less common in childhood, and first infection with tubercle bacilli correspondingly commoner in the years of adolescence and adult life. In the most recent edition (1940) the designation by types is omitted, and primary and reinfection "phases" are distinguished, a change seemingly intended to avoid the previously implied distinction of virtually separate diseases.

In this manual, primary tuberculosis is described as follows: The disease begins as a single or, more rarely, multiple parenchymal lesion in the lower-lung or middle-lung field, with involvement of the hilar lymph nodes. Encapsulation and calcification constitute the prevalent type of retrogression, and lymphatic and hematogenous dissemination, or spread by direct continuity, the prevalent type of progression. Reinfection-type tuberculosis, on the other hand, is pictured in the

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following manner: The initial lesion is a parenchymal focus, usually in the upper third of the lung, without gross involvement of the hilar lymph nodes. Retrogression commonly occurs by resorption and fibrosis. Progression takes place by caseation, liquefaction, excavation and bronchogenic spread.

There is no disagreement on the anatomic character and clinical course of primary and reinfection-type tuberculosis in so far as they occur typically in children and adults, respectively. There is divergence of opinion, however, in other important respects. Dispute centers largely on the following questions: the character and prognosis of primary tuberculosis in adolescents and young adults, the source of infection in reinfection-type tuberculosis in adults, and the role of allergy and immunity in the pathogenesis of reinfection-type tuberculosis.

First-infection tuberculosis, as it occurs typically in children, is obviously exogenous. We may dismiss almost without comment the question of the type of tubercle bacillus concerned. Virtually without exception in the United States, where bovine tuberculosis has been almost eradicated, infection is with human-type tubercle bacilli. It is usually not grave in children, although this statement requires some qualification with regard to Negro children. In the latter, as in white children, in the great majority of cases first infection does not lead to progressive disease; however, lesions that do progress are commoner in Negro than in white children, and greater caution is necessary in the former in estimating prognosis and prescribing treatment when early lesions of first infection are discovered. In both white and Negro children the lesion may occur in any part of the lung, and usually, when the infection is sufficiently intense to be represented by a shadow easily seen in the x-ray film, the tracheobronchial lymph nodes are enlarged. If necrosis of tissue in the lesions of the lung and lymph nodes occurs, the recovery which typically follows is accompanied by calcification of the injured area. In the relatively uncommon cases where the disease progresses, it does so by expanding infiltration of the lung, by ulceration of a tuberculous lesion of a lymph node into a bronchus, with tuberculous pneumonia in the lung parenchyma of the tributary bronchial branches, or by vascular involvement leading to generalized tuberculosis.

In adolescents and adults, on the other hand, first infection with tuberculosis does not appear to follow any well-recognized pattern. Indeed, the claims of various investigators as to the type of response can hardly be reconciled. Some assert that in anatomical character and clinical course, in which it is generally benign, primary tuberculosis in adults is quite like that in children. Others state that the disease is anatomically like that typical of first-infection tuberculosis in children, but that the lesions are more prone to be progressive. A third group holds that the disease anatomically is unlike that characteristic of primary tuberculosis in childhood, having a tendency to conform with the typical reinfection tuberculosis in adults, but that it is clinically of the same benign, non-progressive character that is the rule in children. A fourth group does not agree with any of the others, insisting that primary tuberculosis in adults is both anatomically and clinically unlike first infection in children, resembling reinfection-type tuberculosis in its tendency to apical pulmonary infiltration without involvement of the lymph nodes, and exhibiting a strong tendency to progressive extension with unfavorable outcome.

Knowledge of the truth is of great importance in view of the inescapable fact that primary tuberculous infection in adults, once rare because of the near universality of exposure in early life, is now becoming common. Perhaps a partial answer to the question lies in the fact that in spite of the present frequent postponement of first infection to late years, no unusual incidence of acute or progressive tuberculosis has become apparent. More studies on the subject are desirable. One such, under way at the moment at the Henry Phipps Institute, has disclosed that all the possible varieties of first-infection tuberculosis in adolescents or adults listed above may occur, and indeed that there may be a number of sub-varieties, but that in the limited material available there has been no indication of a preponderance of any one type.

The second disputed problem in the list enumerated above is the source of infection in the characteristic reinfection-type tuberculosis of adults. Up to a decade and a half ago the view most widely held was that this form of tuberculosis is endogenous, the bacilli concerned in the progressive lesion of middle life being mobilized, as a result of some one of a variety of strains, from a previous latent but unhealed lesion of primary type contracted many years before. The last fifteen years have witnessed a sharp reversal of this concept, and wide adoption of the view that reinfections are like first infections in that they are acquired from without, the exogenous superinfection overcoming whatever increased resistance to small doses of tubercle bacilli was conferred by the original or any subsequent non-progressive infection.

A large amount of evidence for this etiology has been brought forth. The well-known studies of Opie and McPhedran[1] have shown that the anatomically characteristic reinfection-type tuberculosis develops much more frequently in previously healthy people in contact with open cases of tuberculosis than it does in previously healthy people not in contact with open cases, even though the two groups may be alike with respect to the possession of old healed lesions of first-infection-type tuberculosis.

On the other hand, because of the increasingly common serial use of x-ray films in cases detected in the early stages of primary infection and followed for years, with final observation at necropsy, evidence is accumulating that characteristic primary lesions may develop, smolder for years with occasional small extensions to other parts of the lungs, and finally mature as progressive tuberculosis of the anatomical type commonly accepted as being of reinfection character. Sweany,[2] in particular, has written of such cases.

Proof of endogenous development of reinfection-type tuberculosis years after the acquisition of primary tuberculosis is almost impossible, because the possibility of subsequent infection can almost never be ruled out. On the other hand, the abrupt transition from health to progressive disease in patients in contact with open tuberculosis and judged previously to have been infected, because of the presence of calcified lesions or a positive tuberculin reaction of some years' standing, is common, and is convincing for exogenous infection. Some of the best examples have come from the study of tuberculosis in married couples, where a healthy person, with evidence of old healed tuberculosis, develops fresh active disease shortly after marriage to a patient with open tuberculosis.

Evidence against the theory of endogenous development is accumulating in the repeated demonstration that the old foci of primary tuberculosis after dense fibrosis and calcification have occurred no longer contain viable tubercle bacilli (Feldman and Baggenstoss[3]). The just claim has been made, however, that small lesions secondary to the main primary lesion are numerous, and it is impossible to examine all of them for sterility (Pinner[4]). However, it seems unlikely that the main lesion would heal completely and minor ones remain infectious. On the whole, the distinction between endogenous and exogenous reinfection seems to resolve into that between slowly and often very irregularly progressive primary tuberculosis, often lasting years before it leads to clinical disability, and fresh disease of abrupt onset resulting from new infection from an outside source.

The difference in anatomic character between primary tuberculosis and reinfection tuberculosis, as they are ordinarily observed in children and adults, respectively, is great. The latter type arises almost exclusively in the upper part of a lung, whereas the former may take origin in any part. In the ordinary reinfection tuberculosis of white persons the hilar lymph nodes are not grossly involved, even when the disease has invaded most of the lung parenchyma. Microscopic involvement of these nodes occurs almost constantly, however, and an exception to the rule occurs in Negro patients; in them, even when the reinfection character of the lesion is thoroughly established by the presence of an unmistakable healed primary tuberculous lesion, gross involvement of the hilar nodes is not uncommon.

Attempts have repeatedly been made to explain the difference in anatomic response in primary and reinfection tuberculosis on immunological grounds. The first infection takes place in tissue not sensitized by the previous presence of tubercle bacilli. The phenomenon of allergy is absent. In reinfection tuberculosis, on the other hand, tubercle bacilli, present long before, have sensitized the tissue. Infection under the two conditions has been likened to experimental skin tuberculosis in normal and previously infected guinea pigs. In these animals in the one case an indolent process occurs, not very conspicuous in the first few days, but spreading slowly and ultimately involving the regional lymph nodes, while in the other there is an explosive reaction with ulceration, the so-called "Koch phenomenon," with less tendency to involve the tributary lymph nodes. The excavation of reinfection tuberculosis has by some been considered as analogous to the ulceration of the latter.

Actually, however, the resemblance in the two cases is rather remote. Tuberculous infection of the skin of normal guinea pigs, while slow in evolution, is progressive in development, whereas first infection in children commonly progresses for a few months and then regresses. Its relations to allergy are complicated. Absent in the beginning, allergy develops a few weeks after infection, while the lesion is progressive. It appears to reach its peak about the time of maximum development of the lesion (Johnston, Howard and Maroney[5]), and to recede as the latter regresses. It is difficult to distinguish which is cause and which effect, however. Certainly tuberculosis is still active in a stage when strong allergy is pres-

ent, and the latter has no tendency to convert the lesion to excavating tuberculosis characteristic of the reinfection type.

Allergy in the ordinary sense of increased tissue reactivity cannot explain the difference between the primary and reinfection types of tuberculosis. In moderately advanced pulmonary tuberculosis allergy is depressed, and yet new lesions forming in the progressive course of the disease have the same fibroulcerative character as have the first lesions of reinfection. The key phenomenon in progressive reinfection-type tuberculosis is liquefaction. Formerly this was explained as being due largely to secondary infection and the proteolytic ferments of the bacteria or the leukocytes attracted by them. However, recent research (Pagel[6]) suggests that it is an independent phenomenon, related in some way to the immunologic state. An Arthus-like phenomenon, dependent on reaction between the caseated tissue, which is in effect a foreign tissue, and plasma antibodies, is postulated by certain investigators (Pagel,[6] Lurie[7]), but clear proof for such a phenomenon is lacking.

In such cases there is always satisfaction in falling back on objective facts, which appear in this case to be as follows: Reinfection-type tuberculosis, regardless of allergy, is usually nonprogressive. The majority of reinfections are small, are met by adequate tissue response and heal. A certain number, presumably those dependent on excessive dosage, are progressive. Liquefaction is the most significant pathologic process in progression. Bacilli are numerous in liquefying regions (Long[8]), and drainage of liquefying areas results at the same time in excavation and bronchogenic spread to previously healthy parts of the lungs, where the sequence may be repeated. If the liquefaction process occurring in caseous tuberculous tissue were understood, the nature of progressive tuberculosis would be more nearly apparent.

The subject cannot be dismissed without some reference to the difference between allergy and immunity. There is evidence that allergy may be abolished by desensitization, while increased resistance to infection persists (Rich[9]), and also that allergy may wane with healing while increased resistance remains independently. The question may be raised if the latter, rather than allergy, determines the anatomic character of reinfection-type tuberculosis. This can be answered only by observation of the character of tuberculosis that develops on reinfection in previously infected persons who have lost their allergy. Cases like this have been observed, but no uniformity in the anatomic character of the reinfection is apparent. Israel and Long[10] have seen tuberculosis of three different types develop in patients previously infected primarily who subsequently lost their allergic sensitivity, namely, a lesion quite like typical primary tuberculosis in children, tuberculous infiltration of the type characteristic of reinfection in adults, and pleurisy with effusion.

Finally, the relation between the anatomic character of reinfection tuberculosis and age must be considered. In the past, primary tuberculosis has occurred in children and reinfection tuberculosis in adults. It is a fair question whether primary tuberculosis, if it occurred in adults, might not take on the character of reinfection tuberculosis at the same age. This possibility has already been discussed. A number of investigators have recorded that in their experience primary pulmonary tuberculosis in adults tends to be apical in location with little tendency to affect the tracheobronchial lymph nodes.

It is evident that a good deal more research is necessary for the explanation of the anatomic difference between primary and reinfection tuberculosis. The relations to age are now subject to investigation, since so much first infection now occurs at a period of life in which reinfection tuberculosis is common. If a relation to an immunity that outlasts allergy exists, that, too, should be discovered, since today there are many persons, once infected, who have lost their allergy, through subsidence of the original lesion and lack of subsequent reinfection, and who may yet meet infections of serious intensity.

Summary

There is no disagreement on the anatomic character and clinical course of primary and reinfection tuberculosis as they occur typically in children and adults respectively. There is disagreement, however, on the character of primary infection as it occurs in adults. It is evident that the latter does not always conform to the characteristic picture of first-infection tuberculosis in childhood, but may assume a variety of forms. It is a problem of future research to determine which is the commonest.

Reinfection-type tuberculosis may be either exogenous or endogenous. The exogenous character is more readily susceptible of demonstration than is the endogenous. The frequent abrupt onset of upper-lobe tuberculosis in a person long previously tuberculin-positive and a short time previously in contact with an open case of tuberculosis is acceptable proof for exogenous invasion. Endogenous

pulmonary tuberculosis is chiefly progressive primary tuberculosis, rather than abrupt metastatic tuberculosis dependent on the existence of an old unhealed primary focus.

The anatomic character of reinfection tuberculosis is not necessarily a function of allergy. Allergy is present in the mid-stages of primary tuberculosis, without influencing its course in the direction of reinfection-type tuberculosis. The characteristic feature of progressive reinfection tuberculosis is liquefaction. The latter is the key problem of progressive tuberculosis, and appears to be largely independent of the allergic state, in the accepted sense of the term, although it is probably connected in some way with the immunologic state of the infected person.

7th and Lombard Streets

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DISCUSSION

DR. HENRY D. CHADWICK, Waltham: Dr. Long has stated some of the problems in the pathology of tuberculosis that have been the subject of intensive research by many investigators. Where there is a difference of opinion a clinician may venture to give his impressions, based on observing the behavior of the disease in living subjects. Allergy or sensitivity of the tissues to the presence of the tubercle bacillus develops uniformly following infection, regardless of the age of the individual at the time the infection takes place.

The opportunities for such infections have lessened with the decline in tuberculosis. Since 1900 in Massachusetts the drop in the death rate has been 86 per cent. The incidence of infection is only about half of what it was fifteen years ago. Instead of 40 per cent of high-school students reacting to the tuberculin test only about 20 per cent now do so. This means that 80 per cent of the young people now enter adulthood free from infection. If they become infected afterward they develop primary tuberculosis, or what was formerly called the childhood type.

It is my opinion that the course followed by primary tuberculosis in these cases is not modified except in so far as immunity or resistance is influenced by age. We could express this by saying that the course of primary tuberculosis is dependent on the degree of immunity that is present in an individual at the time the bacillus is implanted. Resistance, however, varies with age. In infancy there is a high degree of susceptibility, and infection occurring in the first and second years of life often results in meningitis or generalized tuberculosis. At from three to ten years of age, resistance is at its highest point. Through adolescence into young adult life susceptibility again seems to increase, as is shown by the climbing death rate, especially in women. After the thirtieth year the deaths in men show a preponderance and the rate for them steadily increases, reaching its peak in the sixties and seventies.

Reinfection tuberculosis doubtless occurs as a result of both endogenous and exogenous infection. I am one of those who believe that the former is the more usual source, and in support of this contention submit the following evidence. A study by Dr. Pope of 850 cases of primary tuberculosis found in the Massachusetts schools in 1924–1928 and reviewed in 1932 showed that 30, or 3.7 per cent, had developed the reinfection type of pulmonary tuberculosis. In a control group of 405 positive reactors of similar age, sex and family contact but without roentgenological evidence of disease at the time of first examination, 3, or 0.7 per cent, developed pulmonary tuberculosis. Thus there were two groups of infected children: one with lesions massive enough to be demonstrated by x-ray, the other with no visible lesions. The former group developed five times as many cases of reinfection tuberculosis as did the latter. The natural inference is that most of them were reinfected from their own foci of disease, as otherwise the two groups were subjected to similar environmental conditions. Again, the average age of men admitted to sanatoriums for treatment is increasing. At the Middlesex County Sanatorium the men admitted during the three years prior to 1939 were on an average five years older than those admitted for a similar period prior to 1935. There are fewer cases of tuberculosis in the State and 4500 of them are hospitalized, thereby keeping that number of foci of infection from spreading the disease in the community. The death rate is declining at the rate of 40 per cent in each decade. Yet the mortality for men from sixty to seventy remains high — in fact it is higher than at any other age period. This must mean that resistance becomes lower with advancing years, and that men fall victims to their own tuberculous focus that they have been harboring for years — probably acquired in childhood. This represents the carry-over from a time when infection with tubercle bacilli was more nearly universal. Otherwise how can we account for the steady climb of the death rate from tuberculosis for the United States in 1937 from 33 per 100,000 in the age group fifteen to nineteen to 104 for the age group seventy-five to seventy-nine, notwithstanding the fact that opportunities for exogenous infection have steadily decreased.

Tuberculosis is a lifetime disease in many cases, with periods of latency alternating with more or less active phases extending over many years. The thing called "resistance" waxes and wanes, and in doing so influences the parasitic existence of the tubercle bacillus; for the host this means varying degrees of health and illness or death. Dr. Long says, "The key phenomenon in progressive reinfection tuberculosis is liquefaction" but acknowledges it is "a process that is not understood." In a few very susceptible individuals the diseased lung is seen literally to melt away as the course of the disease is followed with serial x-ray films.

This type of patient is seen less frequently as the years pass. The breed seems to be dying out and a tougher strain survives. Something seems to be lacking in such individuals which makes one ask whether or not tuberculosis should be classed as a deficiency disease. Some gauge by which resistance can be measured is needed, and some substance or vitamin not yet discovered that can be used to fortify those who are deficient in this essential element, in order to increase their immunity to a degree that will withstand infection.

THE TREATMENT OF PNEUMOCOCCAL PNEUMONIA*

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IT IS a familiar fact that the treatment of pneumococcal lobar pneumonia has been revolutionized within the short period of three years, first by the introduction of the type-specific antipneumococcus rabbit serums by Horsfall, Goodner, MacLeod and Harris,[1] and shortly thereafter by the introduction of sulfapyridine by Whitby.[2] More recently a new sulfonamide derivative, sulfathiazole,[3] has appeared. This compound, reported by McKee, Rake, Greep and van Dyke[4] to be as effective as sulfapyridine in experimental pneumococcal infections, is now being submitted to trial in many clinics. The efficacy of antipneumococcus rabbit serum and of sulfapyridine, either alone or combined, in individual patients, particularly when treatment is initiated early, is well known. Furthermore, sufficiently extensive and consistent statistical data have already been published[5–7] to establish the fact that these methods of treatment possess remarkable curative value, bringing about a notable lowering of case-fatality rates. Consequently it is not the major purpose of this paper to provide further statistical evidence in support of these facts, but rather to discuss some of the problems encountered in the treatment of patients, with particular emphasis on the variations in clinical response which occur. An attempt will be made to analyze some of the factors involved in these variations, and finally our recent experience at the New Haven Hospital with sulfathiazole will be briefly presented.

CLINICAL MATERIAL AND METHODS

The clinical material which forms the basis for this analysis consists of 250 cases of pneumococcal lobar pneumonia treated at the New Haven Hospital between November 30, 1938, and May 1, 1940. Of these, 109 up to January 2, 1940 (Table 1), were treated with sulfapyridine‡ alone and 41 with sulfapyridine and antipneumococcus serum, and 100 between November 30, 1939, and May 1, 1940, with sulfathiazole,§ of which 3 also received serum therapy (Table 2). In the group of 150 patients receiving sulfapyridine there are included 45 under thirteen years of age treated on the Pediatric Service prior to June, 1939. All other patients were over thirteen. No cases have been excluded, whether moribund on admission to the hospital and dying within less than twenty-four hours (5 cases), or dying of some other disease after recovering from pneumonia (3 cases). Comparison of the groups is not statistically valid because of the small numbers and lack of equivalence in the many variables involved, particularly with respect to age distribution and the incidence of severe bacteremic cases.

In general the initial dose of sulfapyridine used at first in the adult patients was 2 gm., as recommended by Evans and Gaisford.[8] Later an initial dose of 4 gm., usually divided into four doses of 1 gm. each at hourly intervals, was used. The

TABLE 1. *Data on Cases of Pneumococcal Lobar Pneumonia Treated with Sulfapyridine and with Sulfapyridine and Antipneumococcus Serum.*

TYPE OF PNEUMOCOCCUS	SULFAPYRIDINE			SULFAPYRIDINE AND SERUM			TOTAL		
	NO. OF CASES	BLOOD CULTURE POSITIVE	DEATHS	NO. OF CASES	BLOOD CULTURE POSITIVE	DEATHS	NO. OF CASES	BLOOD CULTURE POSITIVE	DEATHS
1	17	5	1	17	6	2	34	11	3
2	0	0	0	4	2	1	4	2	1
3	25	0	4	1	0	1	26	0	5
4–8	31	2	1	17	6	2	48	8	3
9–13	5	1	0	0	0	0	5	1	0
14	14	1	1	1	1	1	15	2	2
15–32*	17	0	0	1	0	0	18	0	0
Totals	109	9	7	41	15	7	150	24	14
Percentages		8	6		37	17		16	9

*Including higher types not determined.

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‡The sulfapyridine used was in large part obtained through the courtesy of Merck and Company, Rahway, New Jersey.

§The sulfathiazole used was largely supplied through the courtesy of E. R. Squibb and Sons, New York City, and in part by Merck and Company.

initial dose was followed by 1 gm. every four hours day and night. Appropriately smaller doses were used in infants and children. With sulfathiazole an initial single dose of 4 gm. followed by 1 gm. every four hours was employed. Variations from this general scheme of dosage have been based primarily on blood concentrations outside the usual range, or on other factors, such as persistent vomiting. This scheme has seemed therapeutically effective and has served to establish promptly in the majority of patients a blood concentration ranging between 4 and 10 mg. per 100 cc. Parenteral treatment has been resorted to when severe vomiting has interfered with adequate oral dosage and in stuporous or extremely ill patients. In adults treatment has ordinarily been continued until the seventh to the ninth day of the disease; in children it was commonly stopped by the fifth day.

In the sulfapyridine-treated group, serum therapy was combined with chemotherapy in 41 cases, the serum usually being given as soon as the type of pneumococcus was determined, in a single dose or in two divided doses totaling 100,000 to 300,000 units, depending on the duration and estimated severity of the disease and the type of pneumococcus, according to the plan outlined by Loughlin, Bennett and Spitz.[9] As time went on serum was reserved more and more for the late or obviously very severe cases. In the sulfathiazole-treated group it was used only three times.

For purposes of subsequent analysis, all patients had an initial blood culture and the majority one or more subsequent cultures. Daily determinations of the concentrations of total and free sulfapyridine or sulfathiazole were made in most of the cases. The blood was watched closely for evidences of neutropenia and anemia, the urine for hematuria. A careful record of nausea and vomiting and other untoward reactions was kept.

Clinical Response to Therapy

Obviously the major problems involved at present in the treatment of patients with pneumococcal pneumonia are, first, the choice between serum therapy and chemotherapy; next, decision whether and when combined therapy should be employed; and lastly, if chemotherapy is chosen, whether sulfapyridine or sulfathiazole should be used. Answers to these problems would appear to be still in the realm of opinion based on individual experience, rather than backed by sound statistical evidence. For this reason the opinions expressed below should be regarded as tentative and subject to modification through the experience of others or further experience of our own.

While it may be generally agreed that the clinical response of patients with lobar pneumonia to treatment with antipneumococcus serum or chemotherapy is in general excellent, it is nevertheless quite variable, and it is these variations from patient to patient that will be discussed as a background for the opinions to be expressed. Since the clinical material dealt with is variable with respect to certain determinable factors such as type of pneumococcus, age, day of disease when treatment was started and presence or absence of bacteremia, the possible influence of these on variations in clinical response will be analyzed. In the analysis the toxic reaction of nausea and vomiting will be disregarded. The problems presented by this and other untoward reactions to serum or sulfonamide compounds will be analyzed separately. The response to therapy will be divided into initial response and subsequent course. The data are summarized in Tables 3, 4 and 5.

Patients Treated with Sulfapyridine Alone

The most frequent type of clinical response encountered in the 109 patients treated by sulfapyri-

Table 2. *Data on Cases of Pneumococcal Lobar Pneumonia Treated with Sulfathiazole and with Sulfathiazole and Antipneumococcus Serum.*

Type of Pneumococcus	Sulfathiazole			Sulfathiazole and Serum			Total		
	No. of cases	Blood culture positive	Deaths	No. of cases	Blood culture positive	Deaths	No. of cases	Blood culture positive	Deaths
1	30	7	1†	2	2	2†	32	9	3†
2	1	0	0	0	0	0	1	0	0
3	17	2	1	1	0	0	18	2	1
4–8	21	6	0	0	0	0	21	6	0
9–32*	28	0	0	0	0	0	28	0	0
Totals	97	15	2	3	2	2	100	17	4
Percentages								17	4

*Including higher types not determined.
†Bacteremic.

dine alone (Table 3) was recovery by crisis within approximately twenty-four hours after initiation of treatment and an uneventful convalescence, occurring in 55 cases (50 per cent). The second type of response was prompt recovery by rapid lysis within forty-eight hours and an uninterrupted convalescence; this occurred in 14 cases (13 per cent). In these two groups, totaling 63

TABLE 3. *Variations in Clinical Response Shown by Patients Treated with Sulfapyridine Alone.*

INITIAL RESPONSE	SUBSEQUENT COURSE	NO. OF CASES	PER CENT
Recovered cases			
Crisis	Convalescence uneventful	55	50
Lysis	Convalescence uneventful	14	13
Crisis or lysis	Low fever, 2 to 10 days	12	11
	Relapse	4	4
	Infectious complication	3	3
	Toxic drug reaction	13*	12*
None	Toxic drug reaction	1	1
		102	94
Fatal cases			
Crisis	Agranulocytosis	1	1
Temporary or none		6	5
		7	6

*Plus 4 cases in other groups: 17 (16 per cent).

per cent, the response may be said to have been highly satisfactory and to have offered no particular problems. Obviously the addition of serum therapy was not indicated.

The third type of response consisted of an initial rapid improvement by crisis or lysis, followed by a low-grade fever ordinarily ranging between 100 and 101°F. (rectal) for a few days to a week or more without apparent cause. Ultimate recovery occurred without any infectious complication or delayed reaction to the drug. There were 12 cases in this group. They represent a type of case which must be carefully watched and is sometimes puzzling.

Another variation in clinical course following apparent initial recovery was relapse, with fever and physical signs indicating spread of the pneumonia. This occurred in only 4 cases: in 1 after two days of normal temperature while the patient was still under treatment; in 3 following discontinuance of sulfapyridine. The major problem presented by this occurrence is that of distinguishing between relapse of infection and drug fever. Our experience indicates that, unless it can be proved otherwise, the sudden recurrence of fever after a few days of essentially normal temperature should be tentatively regarded as drug fever and chemotherapy should be stopped.

In 3 cases apparent convalescence was interrupted by an infectious complication. These were a sterile serofibrinous pleural effusion of ten days' duration, requiring drainage by thoracentesis, an organizing pneumonitis and lung abscess associated with a superimposed staphylococcal infection, and an empyema requiring surgical drainage. All the patients recovered.

Still another variation in clinical course following a satisfactory initial response was that due to untoward reactions to sulfapyridine itself. This occurred in 13 cases with an otherwise uneventful subsequent course, and in 4 which are included in other groups, making a total of 17 cases (16 per cent). These are discussed further below.

Only 1 patient (aged sixty-three, Type 3, treated on seventh day) in the recovered group showed no apparent initial response, perhaps because of the prompt development of hepatitis, followed by drug fever with rash.

The final group consists of 7 fatal cases (6 per cent). One of these patients, a woman of sixty-one with advanced Paget's disease and a Type 4 pneumococcus pneumonia, recovered promptly from the pneumonia but subsequently developed agranulocytosis on the twenty-second day, from which she died three days later. The data on the other 6 fatal cases are as follows:

M. S., aged 70; arteriosclerotic heart disease, asthmatic bronchitis and emphysema; treated on 5th day; Type 1, bacteremic; died 10th day.

A. A., aged 83; treated on 4th day, Type 3, bilateral; died 7th day.

I. K., aged 74; arteriosclerotic heart disease; treated on 5th day; Type 3, bilateral; died 9th day.

J. P., aged 55; arteriosclerotic heart disease and congestive failure; treated on 6th day; Type 3, bilateral; died 12th day.

J. L., aged 75; severe bleeding peptic ulcer; treated on 2nd day; Type 3; died 7th day.

S. D., aged 67; arteriosclerotic heart disease and congestive failure; treated on 4th day; Type 14, moribund; died 5th day.

The obviously noteworthy fact is that there were no deaths in patients under fifty-five years of age, and that fatalities occurred for the most part among those who suffered from severe chronic disease.

Analysis of the relation of the type of pneumococcus to the variations in clinical response shows a significant difference only in the case of Type 3 infections. While the percentage of all other types showing prompt clinical recovery by crisis or lysis (inclusive of those with toxic drug reactions) ranged from 82 to 86, it was only 48 per cent in the Type 3 cases. Consequently the percentage of Type 3 patients showing low-grade fever following an initial favorable response, relapse or death

was considerably higher than it was in the other types. That this apparent relative ineffectiveness of sulfapyridine is due to a greater resistance to the action of sulfapyridine on the part of the Type 3 pneumococcus seems improbable, however, when the relation of age to clinical response is analyzed and it is at the same time noted that 64 per cent of the Type 3 cases were over fifty years of age.

The influence of age on the clinical response of patients with pneumococcal lobar pneumonia treated with sulfapyridine is important. It is illustrated by the fact that 97 per cent of patients under ten, 75 per cent of those from ten to thirty-nine, 68 per cent of those from forty to fifty-nine, and 48 per cent of those sixty or older recovered by crisis or lysis, with uneventful convalescence apart from drug reactions. Conversely the proportion showing low-grade fever, relapse, complications or fatal outcome steadily rose with increasing age, the figures being 3 per cent under ten years, 25 per cent from ten to thirty-nine, 32 per cent from forty to fifty-nine, and 52 per cent in patients of sixty or over, all the deaths being in patients of fifty-five or over.

The influence of delayed treatment is less conspicuous. Of 69 cases in which treatment was started on or before the third day of the disease, 77 per cent showed prompt recovery by crisis or lysis (including those with toxic drug reactions). Of 40 cases in which treatment was begun on the fourth day or later, the percentage was approximately the same, 73. While it is true that the case fatality rate was only 1 per cent in the cases treated early, as contrasted with 15 per cent in those treated late, it must be pointed out that slightly less than one quarter of the early cases were over fifty years of age, as compared with nearly half the late cases.

In this series the influence of bacteremia appears unimportant, but the number of bacteremic cases is too small to warrant analysis. Six of the 7 patients recovered, the fatal case being a Type 1 pneumonia in a man of seventy, admitted on the fifth day of the disease.

Patients Treated with Sulfapyridine and Antipneumococcus Serum

The variations in clinical response to combined therapy — sulfapyridine and antipneumococcus serum — were in general quite similar to those in patients treated with sulfapyridine alone, with the addition of serum disease, which occurred in approximately one third of the cases. The data are summarized in Table 4, from which it will be seen at once that while a much lower proportion of patients recovered promptly and uneventfully than was the case in the patients treated with sulfapyridine alone, a much higher proportion presented complications or died.

The complications encountered in this group were as follows: sterile pleural effusion (1 case); empyema (4 cases); organizing pneumonitis with abscess (2 cases); thrombophlebitis (1 case); and possible cerebral arteritis with hemiplegia (1 case). All the patients recovered except one of those with empyema. With one exception, a patient of thirty-

TABLE 4. *Variations in Clinical Response Shown by Patients Treated with Sulfapyridine and Antipneumococcus Serum.*

Initial Response	Subsequent Course	No. of Cases	Per Cent	Total Per Cent
Recovered cases				
Crisis or lysis	Convalescence uneventful	11	27	
	Low fever, several days	4	10	(+3) 17
	Toxic drug reaction	2	5	(+1) 7
	Serum disease	7	17	(+6) 32
Temporary improvement	Infectious complication	8	20	(+1) 22
None to serum	Recovered with sulfapyridine	1	2	
None to sulfapyridine	Recovered with serum	1	2	
		34	83	
Fatal cases				
Crisis or lysis	Died, other disease	2	5	
Temporary or none		5	12	
		7	17	

two with advanced rheumatic heart disease admitted moribund with a Type 1 bacteremic pneumonia, the patients who died were over fifty-eight years of age and subject to more or less severe chronic disease.

While the two groups are comparable with respect to the day of the disease on which treatment was started and in the proportion of patients over fifty, the combined-therapy group included proportionately many fewer children under ten (10 per cent *vs.* 33 per cent) and many more bacteremic cases (37 per cent *vs.* 6 per cent) than did the group treated with sulfapyridine alone. As already pointed out, these differences make comparison invalid.

Patients Treated with Sulfathiazole

There are 100 patients in the sulfathiazole-treated group, including 3 who also received antipneumococcus rabbit serum. The latter are included since serum was not given at once, as was done in nearly all the sulfapyridine-treated group, but later when it seemed possible that sulfathiazole alone would not control the infection.

The data concerning initial response and subsequent course are shown in Table 5, from which it will be seen that they fall into the same categories as do the previous groups. The patients recovering promptly by crisis or rapid lysis with

uneventful convalescence comprised 55 per cent of the group, approximately equivalent to the corresponding percentage in the sulfapyridine-treated group. The number of cases showing low fever for several days after the initial satisfactory response is somewhat higher, 26 per cent, undoubtedly owing to the absence of children and the higher proportion of patients over forty years of age (65 per cent *vs.* 41 per cent). Relapse occurred in only 1 case, on the tenth day of convalescence, six days after sulfathiazole had been stopped, the patient being

TABLE 5. *Variations in Clinical Response Shown by Patients Treated with Sulfathiazole.**

INITIAL RESPONSE	SUBSEQUENT COURSE	NO. OF CASES	PER CENT
Recovered cases			
Crisis	Convalescence uneventful	37	37
Rapid lysis	Convalescence uneventful	18	18
Crisis or lysis	Low fever, 2 to 10 days	26	26
	Temporary relapse	1	1
	Sterile pleural effusion	4	4
	Toxic drug reaction	6†	6†
Improved	Gradual lysis	4	4
		96	96
Fatal cases			
Temporary or none		4	4

*One recovered case and 2 fatal cases received antipneumococcus serum.
†Plus 1 case in another group: 7 (7 per cent).

a boy of eighteen with a Type 16 non-bacteremic pneumonia. It was immediately controlled by the resumption of sulfathiazole therapy. Four cases developed sterile pleural effusions sufficiently large to require thoracentesis. Two of the patients who died had empyema. The incidence of toxic drug reactions, which were relatively minor in severity, was about half that in the sulfapyridine-treated group. Four patients recovered by gradual lysis over a period of several days.

The number of fatal cases is remarkably small. The data concerning them are as follows:

R. C., aged 46; treated on 2nd day; Type 1, bacteremic; sulfathiazole plus 400,000 units antipneumococcus serum; temporary improvement; serum disease, acute glomerulonephritis, empyema and thoracotomy; died in uremia 39th day.

R. S., aged 50; heart disease with failure; treated on 3rd day; Type 1, bacteremic; sulfathiazole plus 300,000 units antipneumococcus serum; died 66 hours after admission.

R. C., aged 49; advanced hypertensive cardiovascular disease with severe congestive failure, anasarca and cirrhosis of liver; treated on 4th day; Type 1, bacteremic, moribund; died 14 hours after admission.

A. H., aged 62; treated on 15th day; Type 3, non-bacteremic, bilateral consolidation, with empyema and superimposed staphylococcal infection of lungs; died 25th day.

Analysis of the relation of the type of pneumococcus to the variations in clinical response shows the same tendency as in the sulfapyridine-treated group for Type 3 cases to recover less promptly than those due to other types (44 per cent *vs.* 64 per cent), probably owing to the larger proportion of older patients.

The influence of age on the clinical response to sulfathiazole is comparable to that in the sulfapyridine-treated group, 76 per cent of the patients under forty showing prompt recovery by crisis or lysis with uneventful convalescence apart from an occasional drug reaction, as contrasted with 50 per cent of those over sixty. Conversely, the proportion of those showing low fever, slow lysis, complications or fatal outcome rose from 24 per cent in the younger group to 50 per cent in the older one.

The influence of delayed treatment and of bacteremia appears to be somewhat more conspicuous in the sulfathiazole-treated than in the sulfapyridine-treated group, presumably because of the higher proportion of older patients and severe bacteremic cases. Thus, only 45 per cent of the patients treated with sulfathiazole whose treatment was begun later than the third day of the disease recovered promptly by crisis or rapid lysis, as contrasted with 73 per cent in the sulfapyridine-treated group, but 65 per cent of those treated with sulfathiazole were over forty years of age and 17 per cent were bacteremic, against 41 per cent and 7 per cent, respectively, in the sulfapyridine cases.

FACTORS INFLUENCING MORTALITY

A brief analysis of the influence of bacteremia and of age on mortality in the total series of 250

TABLE 6. *Relation of Bacteremia to Mortality.*

TYPE OF THERAPY	POSITIVE BLOOD CULTURE			NEGATIVE BLOOD CULTURE		
	NO. OF CASES	DEATHS	MORTALITY RATE	NO. OF CASES	DEATHS	MORTALITY RATE
			%			%
Sulfapyridine	9	1	11	100	6	6
Sulfapyridine plus serum	15	4	27	26	3	12
	24	5	21	126	9	7
Sulfathiazole	17*	3*	18	83†	1	1

*Two cases received antipneumococcus serum.
†One case received antipneumococcus serum.

patients is presented in Tables 6 and 7. Careful study indicates that, in this series, old age, with its accompanying greater incidence of chronic disease, was a more potent factor than was bacteremia per se. This is well illustrated in the total column in Table 7, in which it will be noted that only

1 (0.8 per cent) of 124 patients under forty years of age, of which 14 (11 per cent) were bacteremic, and only 5 (7 per cent) of 70 patients between forty and fifty-nine, even though 22 (31 per cent) were bacteremic, died, while of 56 patients over sixty, of which only 6 (11 per cent) were bacteremic, 12 (21 per cent) succumbed.

The influence of delayed institution of treatment (Table 8), as might be expected, appears to be considerable. The case fatality rate in 166 cases in which treatment was begun on or before the third day of pneumonia was 4 per cent, while it was approximately three times as great, or 13 per cent, in the 84 cases admitted to the hospital on or after the fourth day. This difference in mortality between the early and late cases, however, is probably largely dependent on the important factor of age, as careful analysis of the data in Table 8 will show. Of the 166 early cases, 58 per cent were under forty years of age, as contrasted with only 33 per cent of the 84 late cases. Bacteremic cases were equivalent in the early and late cases — 16 and 17 per cent, respectively.

Table 7. *Relation of Age to Mortality.*

Age	Sulfapyridine-Treated Cases*			Sulfathiazole-Treated Cases*			Total		
	No.	Deaths	Mortality Rate	No.	Deaths	Mortality Rate	No.	Deaths	Mortality Rate
yr.			%			%			%
Below 10	40^{2}†	0	0	0	0	0	124^{14}	1^{1}	1
10–19	18^{4}	0	0	10^{1}	0	0			
20–39	31^{5}	1^{1}	3	25^{1}	0	0			
40–59	29^{9}	2^{1}	7	41^{13}	3^{2}	7	70^{22}	5^{3}	7
60–89	32^{4}	11^{3}	34	24^{2}	1	4	56^{6}	12^{3}	21

*Forty-one of the sulfapyridine-treated cases and 3 of the sulfathiazole cases received antipneumococcus serum.
†Exponents indicate bacteremic cases.

Table 8. *Relation of Time of Beginning Treatment to Mortality.*

Age	Treatment Begun First to Third Day			Treatment Begun Fourth Day or Later		
	No. of Cases	Per Cent	Deaths	No. of Cases	Per Cent	Deaths
yr.						
Under 40	96^{12}*	58	1^{1}	28^{1}	33	0
Over 40	70^{15}	42	6^{3}	56^{12}	67	11^{4}
Total	166^{27}		7^{4} (4%)	84^{14}		11^{4} (13%)

*Exponents indicate number of bacteremic cases.

Reactions Due to Treatment

The immediate and later untoward reactions associated with serum therapy and with sulfapyridine therapy are so well known that they are not described in detail here. It seems of interest, however, to compare sulfapyridine and sulfathiazole in this respect in so far as our experience permits.

The most distressing early toxic effect of sulfapyridine is nausea and vomiting. In this series, excluding the patients under thirteen years of age for better comparison with the sulfathiazole-treated group, vomiting occurred in 72 per cent, being mild in 20 per cent, moderate in 20 per cent, severe in 21 per cent and extremely severe in 11 per cent. The incidence of vomiting in the sulfathiazole-treated cases was conspicuously less, 55 per cent not vomiting at all. Mild vomiting occurred in 21 per cent, moderate in 11 per cent, severe in 10 per cent and extremely severe in 3 per cent. Not only the vomiting was much less, but also the accompanying sense of nausea, mental depression and irritability.

The comparative incidence of the late drug reactions in the sulfapyridine-treated and sulfathiazole-treated groups is shown in Table 9. The apparent advantage of sulfathiazole may be only a matter of chance, which a larger series will modify. Conspicuous, however, is the absence of gross hematuria with renal colic and oliguria or temporary anuria, which occurred in 3 cases in the sulfapyridine-treated group. So far, only very occasional, transient microscopic hematuria has been encountered in our patients treated with sulfathiazole, and no case of acute hemolytic anemia or agranulocytosis. Maculopapular rashes and conjunctival injection have been seen in other patients, but did not occur in this group.

Table 9. *Late Drug Reactions.*

Reaction	No. of Sulfapyridine-Treated Cases*	No. of Sulfathiazole-Treated Cases
Drug fever	4	4
Drug fever and rash	6	0
Hemolytic anemia	1	0
Neutropenia	2	1
Agranulocytosis	1	0
Hematuria		
Microscopic	2	2
Gross	3	0
Hepatitis	1	0
Totals	17 (16%)	7 (7%)

*Cases receiving antipneumococcus serum not included.

Another advantage possessed by sulfathiazole over sulfapyridine is the relatively moderate degree of conjugation to the acetyl derivative,[10] sulfathiazole being similar to sulfanilamide in this respect, since the usual range of acetylation is between 5 and 30 per cent. For this reason determination of total sulfathiazole blood concentrations is not so necessary as in the case of sulfapyridine,[11] knowledge of the concentration of free sulfathiazole being adequate for practical purposes.

Summary

Observations on the treatment of pneumococcal lobar pneumonia with sulfapyridine, combined sulfapyridine and antipneumococcus serum, and sulfathiazole, with special emphasis on the variations in clinical response encountered, are presented.

The results recorded indicate that chemotherapy alone is adequate to bring about prompt recovery in nearly all patients under forty years of age. For this reason it is regarded as the method of choice in this group, and there would appear to be no reason to combine serum with it, certainly in patients coming under treatment early after onset.

In the later decades of life chemotherapy, although less adequate, is nevertheless often remarkably efficient, except in patients suffering from severe chronic disease. In early cases it seems to be at least as valuable as antipneumococcus serum.

While the comparative data in this series are not adequate to establish the fact, our impression is that chemotherapy alone is more effective in late, severe bacteremic cases than is serum therapy alone. While the observations do not provide evidence that combined therapy is more effective in this group, it nevertheless seems advisable in selected cases to give serum in addition to chemotherapy, at least until more adequate comparative statistical data are available.

If chemotherapy is used, sulfathiazole appears at present to be the compound of choice, for the following reasons: It is at least equal to sulfapyridine in therapeutic effectiveness, one of the most striking evidences of this being found in the fact that in all but 3 of the bacteremic cases, with colony counts ranging up to 320 per cubic centimeter of blood, the blood was freed of pneumococci within eight to twenty hours, and in the remaining 3 within forty hours; its use is attended by conspicuously less nausea, vomiting and mental depression; other untoward reactions are less frequent and severe; and the problem of excessive acetylation is not encountered.

Analysis of some of the factors affecting the character of clinical response to chemotherapy has been made. Of these, the type of pneumococcus involved appears to be of little significance. Bacteremia per se, which is probably little more than a measure of severity, rather than a determining factor in outcome, does not appear to be so important as is often supposed. Delayed institution of treatment is attended by less satisfactory results than is early treatment. The most significant factor, however, is age, the majority of cases in this series that failed to show prompt recovery and eventually had complications or complete lack of response with fatal outcome occurring among patients over fifty, particularly those with chronic disease.

Conclusions

Chemotherapy appears to be the method of choice in the treatment of pneumococcal lobar pneumonia. Sulfathiazole seems to possess a number of advantages over sulfapyridine. Treatment should be started as soon as the diagnosis is made. Serum therapy may properly be added to chemotherapy in late, severe cases presumed to be bacteremic. A considerable proportion of unsatisfactory responses may be expected in old persons, particularly in those with chronic disease, although the results will be better in this group than they would be without chemotherapy.

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OSTEOMYELITIS OF THE COCCYX AND SACRUM WITH SINUS FORMATION SIMULATING ANORECTAL FISTULA*

Report of Two Cases

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INFECTIONS of the perineum are surgical conditions of common occurrence, which, in an age of certified specialization, may be seen by any one of several types of specialist. They include rare abscesses, pointing in the perineum, from ruptured appendices,[1] and caries of the pelvic bone.[2–4] It is the purpose of this paper to present two unusual cases which were cured only after localization of the infective process in the lower portion of the vertebral column.

CASE 1. M. B., a 17-year-old Negress, was admitted to the Proctologic Service of Temple University Hospital on November 30, 1938, with a provisional diagnosis of tuberculous fistulas. The patient described a creamy discharge from the anal region of 5 months' duration. Prior to admission she was treated by "needles" by her family physician. The rest of the history was irrelevant.

Examination showed the presence of two external openings, both posterior to the anal verge and approximately 1 cm. from it; one was located in the midline, and the second slightly to the right. The appearance of the openings was in no way unusual. An area of induration surrounded each, but could not be traced digitally as it seemed to be lost in the tissues of the anococcygeal region. On introducing a probe into each aperture, the direction was toward the coccyx, and the penetration 1 and 2 cm., respectively. Repeated examination of the rectum showed no internal opening or primary lesion. The general physical examination was negative. Roentgenographic study of the chest and the gastrointestinal tract was negative.

The x-ray report of the lumbosacral spine was as follows (Fig. 1):

> There is a definite defect in the left side of the fourth sacral segment, and the distal end of the sacrum is eburnated and somewhat irregular in appearance. There has been an osteomyelitis of the sacrum, and it is suspected that this process may still be active. There has been loss of bony substance between the sacrum and coccyx, and the latter is angulated acutely in relation to the sacrum.

Further x-ray study consisted of injection of the sinuses with Lipiodol and fluoroscopic examination, but little or no information was gained except that there was no free communication with the rectum.

The red-cell count was 4,430,000, and the hemoglobin 12.5 gm. The white-cell count was 11,250, with 81 per cent polymorphonuclears, 17 per cent lymphocytes, 1 per cent eosinophils and 1 per cent basophils. Blood Wassermann, Kolmer, Kahn and Kline tests were negative. A complement-fixation test for gonococcal infection was negative. The sedimentation rate was 11.5 mm. in 1 hour.

With a provisional diagnosis of sacrococcygeal osteomyelitis, resulting in sinus formation simulating anorectal fistulas, operation was performed by one of us (H. E. B.) under Avertin and nitrous oxide anesthesia. By careful probing and injection of methylene blue in Petrolagar, the sinuses were found to extend directly to the coccyx and sacrum. Both tracts were widely excised, and the coccyx and lower sacral segment were removed. The wound was left open and permitted to heal by granulation.

FIGURE 1.

Gross section of the tissue showed no cystic formation. The microscopic report was as follows (Fig. 2):

> The epithelium is hyperplastic with increased surface keratinization. The epithelial pegs are distorted and elongated; the corium is thick and sclerotic. There is a perivascular mononuclear cellular infiltration, the predominant cells of which are plasma cells. Some thickening of the vessel walls is noted. Another section of the corium shows chronic granulation tissue with proliferative fibrosis and cellular infiltration. Most of the cells are plasma cells. Sections of bone show some necrosis of the spicules, and infiltration of the marrow with fat and a chronic inflammatory reaction of the periosteum as well as of the bone. There is no

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evidence of tuberculous infection. Diagnosis: chronic inflammation and osteomyelitis.

Following operation the wound was packed lightly with dichloramine-T gauze. A heat cradle was employed and ultra-violet light therapy given each day. The patient was discharged to her family physician 17 days after operation. The wound was completely healed 6 weeks later. According to the physician, the patient has offered no complaints.

FIGURE 2.

CASE 2. G. R., a 42-year-old Negro, was seen in the Proctologic Clinic of the Graduate Hospital in May, 1937, at which time he complained of a "boil" on the right side of the anus. He gave a history of having had a low-back injury 17 years previously. He had had trouble about the anus for 2 months. One month previously a "boil" opened spontaneously on the left buttock. A diagnosis of horseshoe fistula was made, and operation at that time consisted of incision of the abscess and excision of a portion of a tract on the other side.

Following this procedure the wounds healed, and the patient was free of symptoms until the following October, when he again began to have perianal pain, recurring attacks of swelling and discharge of pus from the perineum. He was readmitted to the hospital in March, 1938. A fistulous tract on the left side was found and excised, but no internal opening was demonstrable.

In April, 1938, the patient was again readmitted because of pain and discharge of pus. An incision through the right tract was made up to the muscle, and a seton of linen thread was inserted through the internal opening and carried over to the right external opening. Two weeks later the patient was readmitted for removal of a fistulous tract. Examination showed two lateral, open, granulating wounds. By this time the course of the disease had aroused suspicion, and the coccyx was x-rayed; it showed "an irregularity in the second coccygeal segment suggestive of a localized osteomyelitis." Operation at this time consisted of fistulectomy from the right to the left internal opening.

Following this operation the patient continued to have intermittent attacks of perianal pain and almost constant discharge until seen in the clinic in January, 1939. General physical examination revealed some changes in the left pulmonary apex suggestive of tuberculosis. X-ray study showed chronic tuberculous changes in both lung fields, with a possible area of activity in the left apex. Local examination of the perineum presented a discharging sinus on each side of the anus slightly to the posterior phase and marked deformity of the parts, due to extensive scarring. There was tenderness on palpation of the coccyx. The sinuses could be made to exude a watery fluid on pressure over them. A probe when inserted into the tracts passed posteriorly and impinged on bone, but no suggestion of extension toward the rectum or anus was noted.

The urine was negative on three examinations. The sputum was negative for tubercle bacilli on four occasions. The red-cell count was 4,120,000 and the hemoglobin 11 mg. The white-cell count was 6900. The sedimentation rate was 85 mm. A Wassermann test was strongly positive, a Kahn test moderately positive, and an Eagle test slightly positive. The blood-sugar content was 85 mg. per 100 cc., the urea nitrogen 9 mg. and the van den Bergh 0.2 mg. (indirect).

X-ray examination of the spine was reported as follows: "There has been further bone destruction of the coccyx, and the lower segment of the sacrum shows demineralization, especially on the left. It is probably due to an osteomyelitis with bone necrosis."

Operation was performed by one of us (H. E. B.) on January 19, 1939, under spinal analgesia, employing 60 mg. of Spinocaine in the fourth lumbar interspace. The fistulous openings were explored and found to have no communication with the rectum or anus, but to extend directly to the bone. With the probe in situ against the bone, an elliptical incision was made with the endotherm needle encircling the probe and all tissue down to the coccyx. The prevertebral pelvic fascia was freed from the coccyx, exposing the retrorectal space, and the coccyx was removed. The lower sacral segment was trimmed with a rongeur, and the roughened surface curetted. A small sinus on the right side of the anus was excised, curetted and drained, after which the entire cavity was packed loosely with iodoform gauze for 24 hours. The wound was dressed daily for 3 weeks, and graduated doses of ultraviolet light were administered. By March 15 the wound had filled in completely and was almost epithelialized, there being an area about 7 cm. long and 2 cm. wide. The patient had gained 14 pounds in weight at this time, and his general condition was greatly improved.

The pathological report of the tissue removed stated:

> In the soft tissue there is a fistula lined with granulation tissue. Most of the extensive cellular exudate is such as one sees in an ordinary purulent infection, but in this case it is due to a mixed infection, for a few tubercles exist, and in one of these tubercle bacilli are present. The bone trabeculae are necrotic. The marrow spaces contain much blood, marrow cells and many polymorphonuclear leukocytes. Diagnosis: tuberculous lesion with secondary mixed infection.

According to the literature, osteomyelitis of the coccyx or sacrum, or both, is a very rare condition. Considerable time has been spent in investigating its occurrence. In 1859, Simpson[5] in a series of lectures on injuries and diseases of the coccyx omitted any discussion of osteomyelitis. Gant[6] cites 4 cases of necrosis of the coccyx with fistula formation, one of which he called anal fistula. He attributed necrosis of the coccyx to trauma, tuberculosis, syphilis or cancer. Yeomans[1] presents trauma as a factor in 80 per cent of his cases of coccygodynia, but none of

these cases showed bone necrosis. Monnier[7] in 1904 reported a case of acute osteomyelitis of the coccyx in a seventeen-year-old girl who presented symptoms at first diagnosed as typhoid fever, while Boland[8] in 1927 described a case of osteitis of the coccyx in which a stricture of the rectum had resulted and was followed by typical formation of a rectal fistula. Blount[9] in 1928 reported a case of chronic osteomyelitis due to *Staphylococcus albus*.

On the subject of tuberculosis of the coccyx very little more has been written. The first available elaboration of the condition specifically in the coccyx was written by Lannelongue[10] in 1888, who at that time pointed out the simulation of the disease to primary anorectal disease in its late stages. The first case reported was presented by Pettit[11] in 1790, while the first operation for the condition is credited to Mott[12] of Mobile, Alabama, in 1844. Makins[13] reported a case in 1888 in which the patient presented symptoms of rectal obstruction and extensive ulceration of the entire perineum. Darrah[14] in 1893 reported 3 cases, all of which had been admitted to his service at the Massachusetts General Hospital as ischiorectal abscesses and fistulas. David[2] in 1924 reported 2 cases and reviewed the literature very thoroughly, being able to find 25 other cases, including those of Darrah.

In its etiology osteomyelitis of the coccyx is no different from osteomyelitis of other bones. The commonest organism is *Staphylococcus aureus,* then *S. albus,* and finally *Mycobacterium tuberculosis*. The pyogenic forms are usually hematogenous in origin, although they have been reported as secondary to other localized infections and also to direct trauma or penetrating wounds. The tuberculous form is always secondary to other tuberculous foci and the infection is hematogenously borne.

Regarding trauma as an etiologic factor, various writers have mentioned injury as a possible exciting factor, though most patients seem to have recognized few symptoms until some time after the trauma. In the 27 tuberculous cases reported up to 1924 there was a history of trauma in 10, dating from three months to six years previous to the onset of symptoms. Our patient with tuberculous infection gave a history of an injury seventeen years previous to the presenting symptoms.

As to the incidence of the disease under discussion, statistics are at a premium. Gant's[6] cases were equally divided according to sex and the age range was from twenty-four to forty. Monnier's[7] patient was seventeen years old and a girl. The cases reported by Boland[8] and Blount[9] were both in men, aged thirty-two and thirty-five. An analysis of the tuberculous infections reported shows 18 males and 10 females, with ages ranging from two and a half years to seventy. Trauma is reported in 11 of the cases and an associated tuberculosis in all.

Pathologically the disease varies with the acuity of the infection and the invading organism. The process begins as a localized infection of the body of the vertebra, then abscess formation and resulting bone caries and necrosis, either fulminating, as in the acute pyogenic type, or insidious, as in the tuberculous variety. The direction of the necrosis has much to do with the eventual localization of the resulting tissue involvement. If the necrosis extends anteriorly, there is a rupture through the periosteum into the retrorectal space, giving rise to signs and symptoms of rectal obstruction varying with the extent of growth of the abscess. This may burrow up or down or even perforate into the rectum. If the necrosis is sufficiently caudad in its beginning, burrowing takes place beneath the subcutaneous tissues immediately adjacent to the anococcygeal raphe, to extend into one or both ischiorectal fossae and to present the typical picture of an abscess in this region. If the necrosis directs itself dorsally, this same condition may ensue, or the abscess thus formed may perforate the skin immediately overlying the infected vertebra and present the appearance of an infected pilonidal cyst. The microscopic picture is the same as with similar lesions elsewhere in the body.

The symptoms of osteomyelitis of the coccyx may be acute or chronic, as in osteomyelitis of other bones. The acute symptoms were at first attributed to typhoid fever in 2 reported cases. The chronic form is insidious in its onset, and is early characterized by backache. All writers emphasize this as the initial symptom, which may be the only one present for a time. Lannelongue[10] believes that this stage simulates *neuralgie sacro-coccygienne ou coccydienne,* which is most common in neurotic or hysterical women. David[2] emphasizes the presence of pain as an important symptom, causing difficulty of locomotion, inability to rise from the sitting position and absence of pain during defecation. Later, and usually after several operations, symptoms and signs develop which cannot be correctly interpreted without a careful history-taking and a thorough examination.

It is rarely before the appearance of these signs that the chronic forms of osteomyelitis of the coccyx are diagnosed. The history may or may not elicit trauma as the initial factor, although this usually antedates the onset of symptoms from

months to years. Pain over a period of several weeks or months is described as being dull in character and aggravated by motion, but without relation to the act of defecation. If seen before fistulas have developed, either spontaneously or as a result of insufficient surgery, examination will reveal either the presence of a localized abscess over the coccyx, a unilateral or bilateral abscess of the ischiorectal fossae or even a retrorectal abscess. These are of the "cold" type in the tuberculous form of infection. Bimanual examination of the coccyx either before or after the development of abscess will reveal tenderness of the coccyx, and if the disease has progressed far enough there may even be crepitus of the segments due to the presence of bony fragments resulting from the necrosis. If fistulas have already developed, these are usually draining intermittently. The drainage will vary from purulent material such as that found in staphylococcal infections to the clear, watery or serosanguineous fluid associated with tuberculosis. By proper staining methods[15] the underlying organism may be detected, although usually at this stage of the disease secondary invaders are present. A roentgenogram is of great value and should be taken in every case of persisting sacrococcygeal backache and coccygodynia.

Stafford[16] in 1832 admitted that he had seen an abscess connected with diseased vertebrae show itself in the loins, and in one or two cases in the nates. Autopsy of the case reported by Makins[13] showed the primary seat of the abscess to be in the fifth lumbar vertebra. Boyd[17] remarks that, though rare, pus from a psoas abscess may pass into the pelvis and form an ischiorectal or even a gluteal abscess. Yeomans[1] and others have referred to the pointing of an appendiceal abscess in the perineum. Magnusson,[18] writing from Boras, Sweden, reports several cases of osteomyelitis of the ischium with abscesses and fistulas in the gluteal region. He brings into his differential diagnosis the syndrome of sciatica, which must be considered before the clinical symptoms have developed sufficiently to make a diagnosis.

As to the treatment, there seems to be unanimity of opinion. The acute form requires early drainage if extensive bone destruction is to be avoided. Unfortunately, however, the diagnosis is rarely made early enough to allow only this procedure, so that, along with the chronic form, the proper treatment is ample drainage of the area including the sinuses, with complete removal of the infected bone. All loose sequestrums should be removed and necrotic vertebrae excised, and any adjacent vertebral surfaces which show infection superficially should be curetted. The wounds should be left open and allowed to fill in from the bottom with granulation tissue. In all forms except the tuberculous, early institution of hot sitz baths are of great value in promoting healing. In the tuberculous form, localized ultra-violet therapy in increasing doses up to skin tolerance is beneficial as a local tissue stimulant. Any complicating rectal disease such as stricture, rectal fistula or incontinence due to tissue destruction may be cared for after complete healing of the coccygeal wound. Ordinarily, this requires from two to fourteen months, according to the type of infection.

Summary

Two cases of sacrococcygeal osteomyelitis simulating anorectal fistulas have been reported. Even though of rare occurrence, the condition is of the utmost importance in that by careful examination a correct diagnosis may be made, with the avoidance of unnecessary multiple operations and chronic invalidism.

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REPORT ON MEDICAL PROGRESS

EMERGENCY TREATMENT OF FRACTURES

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ONE of the recent advances in the treatment of injured persons has been the great campaign carried on by the American College of Surgeons to improve the transportation of the injured person from the point of accident to the hospital. This campaign has included the education of doctors, medical students, hospital interns, policemen, firemen, members of the American Red Cross and industrial organizations, railroad employees, civilians and Boy and Girl Scouts.

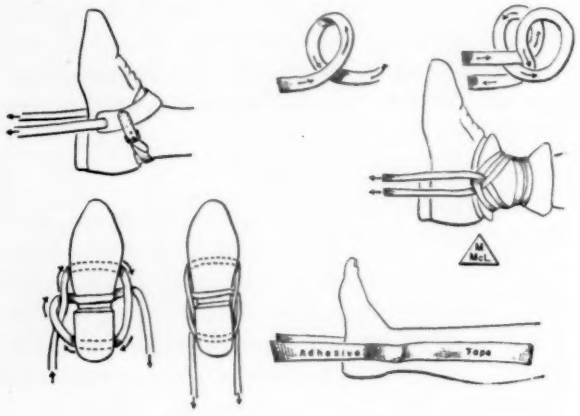

FIGURE 1.

For doctors, demonstrations have been given at state and county medical meetings. Regional fracture committees of the American College of Surgeons have been organized. These plan to include one physician from the staff of every New England hospital. Aided by the Red Cross, members of police departments and industrial organizations have been given careful and thorough training in splinting and transportation. Motion-picture films demonstrating these methods have been made and are available. Splints in proper containers that occupy the minimum carrying space may be obtained at surgical supply houses.

During World War I, the necessity of early splinting was recognized. The same need now exists not only in military but in civilian life. Serious accidents seem to be increasing. The toll from automobile and motorcycle accidents is appalling; industrial accidents continue; and the injuries following sports, particularly skiing, mount yearly.

To meet this need, hospitals have established special wards for the care of the injured. These cases are now assigned to the service of surgeons with particular training in the care of traumatic cases. Once in the hospital, these patients receive proper treatment, but it is in the handling that they receive *before* arrival at the hospital that education and training are most needed.

To quote from *An Outline of the Treatment of Fractures*[1]:

> A man is struck by an automobile, thus breaking his leg. Except for the broken bone, without displacement, the original injury may be merely a slight periosteal tear and a mild contusion of the soft parts, but he is helped to his feet and the leg gives way and the fragments slide by each other, thus stripping off the periosteum and tearing the muscles. He falls to the ground only to be picked up and carried to the sidewalk with the leg dangling. Larger blood vessels are torn and the end of the bone comes through the fascia, perhaps the skin and even the trouser. He is laid at rest with a coat beneath his head and surrounded by people anxious to help. Someone sees that his leg is crooked and straightens it out. The exposed end of the bone re-enters the wound with a bit of trouser and the dirt of the street. He is lifted up and carried to a car or ambulance. This time someone carries the injured leg with better intentions than co-ordination and the ends of the bone are churned around in their bed of lacerated tissues and the contaminating organisms are well disseminated throughout the area. During his ride and in the transfer to the accident ward

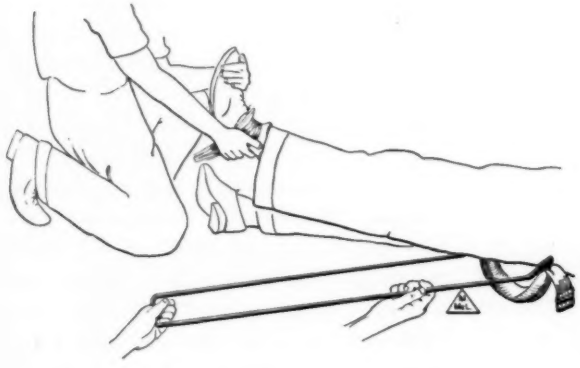

FIGURE 2.

*Assistant in surgery, Harvard Medical School; assistant visiting surgeon, Massachusetts General Hospital.

or the doctor's office, unless he has been carefully splinted, there is more jolting and more damage. Would that his troubles were over, but too often the sad story continues. Lack of sufficient protection as he is lifted to and from the x-ray table and as he is being anesthetized results in still more injury.

Compare this exaggerated picture with a similarly injured man who is allowed to remain where he is until a proper splint can be applied, or at least until he can have someone pull hard on his foot as he is being lifted and carried, whose examination is thoroughly but gently carried out, and whose treatment is instituted with but little additional injury. The difference

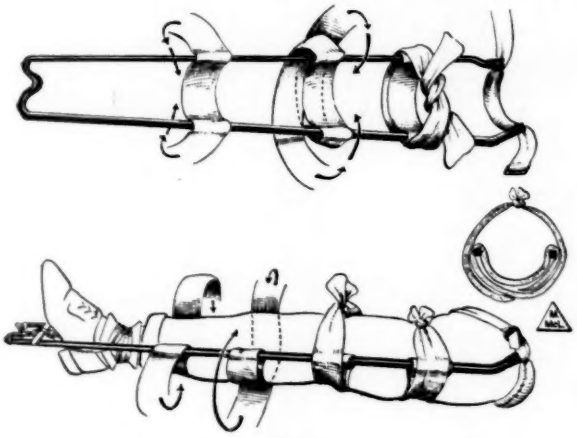

FIGURE 3.

in these two cases as regards periods of disability and amount of permanent functional disturbance is great.

All cases of accident, particularly those to the extremities, should *not* be moved until the injured part or parts have been carefully splinted. Injuries to the spine require special handling.

Transportation, depending on the circumstances, may be furnished as follows:

Ambulances
Police-department vehicles
Fire-department vehicles
Commercial vehicles
Privately owned vehicles
Sleds, toboggans and stretchers
Individuals

An attempt is being made to educate and train all those who might be responsible for transportation.

The necessary splint equipment is as follows:

Keller–Blake leg splint
Murray–Jones arm splint
Stretcher
Triangular bandages (six)
Roller bandages
Sterile dressings and aqueous iodine
Blanket

These are now obtainable in surgical supply houses and can be carried in a small space. When manufactured traction splints are not available, satisfactory fixed traction can be maintained by using notched boards, broomsticks, rakes, branches of trees and so forth. Methods for applying these improvised splints are described in the *American Red Cross First Aid Text-Book*.[2]

Some of the general rules to be followed are as follows:

A splint should always be applied if there is any suspicion of fracture.

The principles of fixed traction and immobilization are used in all splinting.

If there is a wound, paint the surrounding skin with aqueous iodine and apply a sterile dressing.

The splint should be applied where the person falls, *before* moving.

Injuries to the Hip and Leg

A leg splint (Keller–Blake) should be applied. The procedure is as follows:

Cover the patient with a blanket.

Have a helper steady the leg just above the

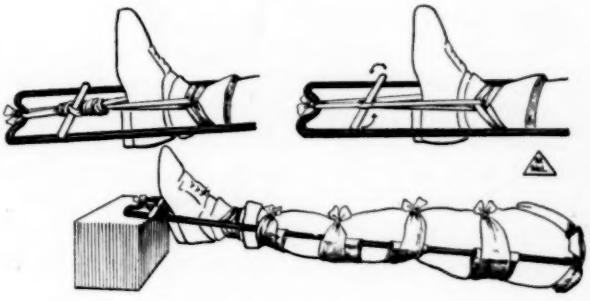

FIGURE 4.

ankle with a firm grip to prevent motion while applying an ankle hitch (Fig. 1):

With bandages and two clove hitches, one on the inner side and one on the outer side
With bandage sling to outside of shoe
With special strap (Army) or laced device about the ankle
With adhesive tape.

Place a firm pull with both hands on the foot and ankle, keeping this up until the splint is fully applied.

Still pulling, raise the injured limb a few inches.

Slip a half-ring splint under the thigh from

the outside, fitting it at the top of the thigh, with the rods lateral (Fig. 2); buckle the groin strap.

Hammock the leg in the splint with four or five cravat bandage or towel slings (Fig. 3).

Tie the extended ends of the ankle-traction hitch over the end of the splint; insert a stick between the ends of the hitch and twist until firm traction is established (Fig. 4).

On a block, elevate the lower end of the splint 6 inches.

Injuries to the Ankle and Foot

A folded blanket or pillow reinforced laterally by thin splint boards all bandaged firmly in place furnishes satisfactory immobilization.

Injuries to the Shoulder and Arm

An arm splint (Murray–Jones) should be applied. The procedure is as follows:

Cover the patient with a blanket.

Have a helper steady the arm just above the wrist with a firm grip to prevent motion while applying a wrist hitch (Fig. 5):

With bandages and two clove hitches, one in front and one in back

With a triangular-sling hand hitch (Red Cross)

With adhesive tape

Place a firm pull with both hands on the wrist, keeping this up until the splint is fully applied.

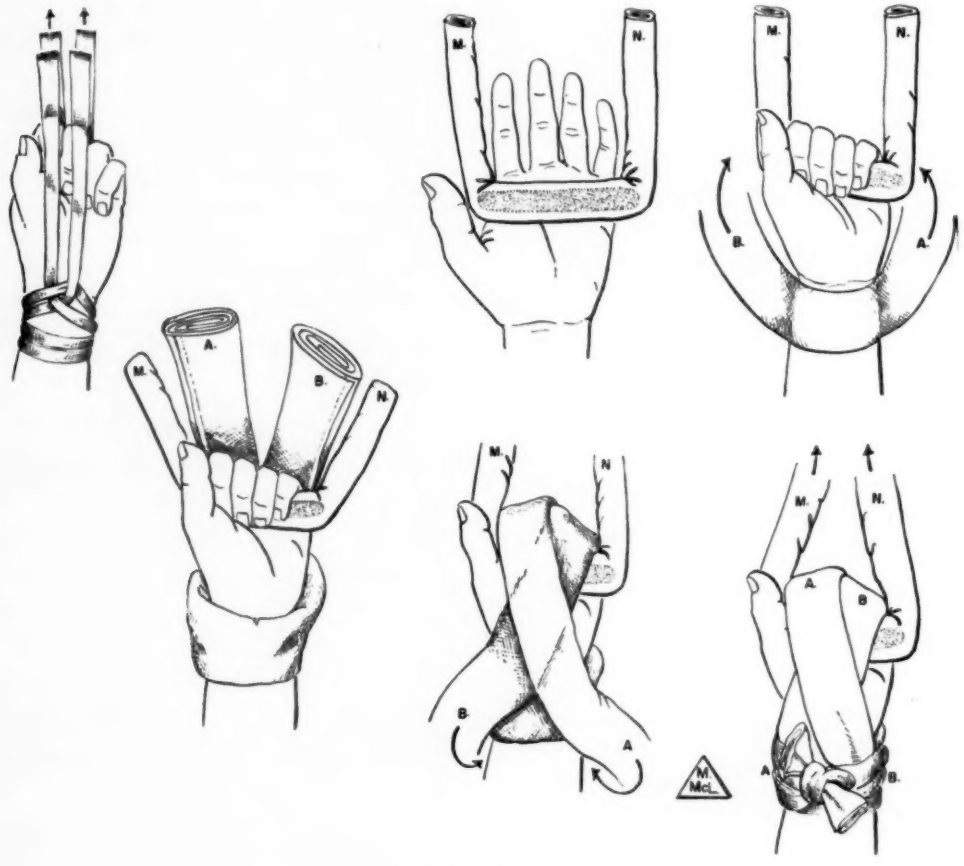

Figure 5.

Thread on the arm splint.

Tie the extended ends of the wrist-traction hitch over the ends of the splint; tighten with a windlass consisting of a stick or nail (Fig. 6).

Hammock the arm in the splint with cravat or bandage slings.

Injuries to the Wrist and Hand

A folded blanket or a well-padded splint board, extending from the elbow to the finger tips and firmly bandaged, plus a sling, furnishes adequate fixation.

Injuries to the Back

To transport a person with an injury to the spine, a rigid litter or stretcher is necessary. This may consist of the following:

A firm stretcher
A wide plank
A door
A toboggan

A blanket should be used for covering.

If the injury is below the shoulders, the patient is usually most comfortable face down, with the head pillowed by the arm (Fig. 7). The injured person should be rolled onto the litter using many

FIGURE 6.

hands and avoiding at all costs even momentary flexion of the spine.

If the injury is above the shoulder, the head

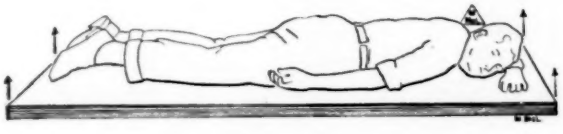

FIGURE 7.

should be steadied by light traction, which can be applied by cupping the head and chin with both hands from above and gently pulling in the line of the body. The patient should be rolled onto the litter face up, in this case avoiding flexion or extension. Steady traction to the head should be maintained during the entire period of transportation (Fig. 8).

If the patient is found lying unconscious, particularly if he shows bruises about the head or face, it is wiser to assume the worst injury—a broken neck—and transport him accordingly.

* * *

Transportation often becomes the duty of civil-

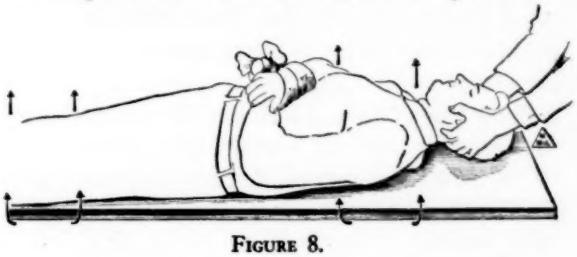

FIGURE 8.

ians. If carried out carefully and thoroughly, the patient will arrive at the hospital in the best possible condition. There is less shock, the pain is less, the broken bones have not overridden, and the healing process is given the chance to proceed normally. Irreparable harm is often done in moving the patient incorrectly from the scene of the accident to the hospital. Immeasurable good is done by proper handling.

Every physician who is not thoroughly familiar with these modern concepts concerning the emergency treatment of fractures should learn them. Some doctors carry traction splints in their cars at all times. All doctors' cars and all ambulances should be so equipped, and the drivers properly trained to use the equipment.

270 Commonwealth Avenue

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2. *American Red Cross First Aid Text-Book*. 248 pp. Philadelphia: P. Blakiston's Son & Co., 1937.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 26431

PRESENTATION OF CASE

A seventy-three-year-old retired silversmith entered the hospital complaining of tenderness in the right lower quadrant of the abdomen of two weeks' duration.

Four years before admission the patient entered the hospital with the classic signs and symptoms of an enlarged prostate. A perineal prostatectomy and bilateral vasectomy were performed, and he was discharged in three weeks, having had an uneventful convalescence. The pathological report was "hyperplasia of the prostate."

During a routine examination two months before admission, pus was found in the urine, and six weeks later, tenderness in the right lower quadrant, which continued until admission.

The patient had broken his arm twice in childhood, and many years before admission he had fractured the head of the left femur, which resulted in limitation of movement of the hip joint. He had had an attack of substernal distress while cranking a car nineteen years before admission and a similar attack nine years before admission. Five years prior to entry the attacks became more frequent on exertion, and the pain sometimes radiated down both arms. His physician restricted his activity and prescribed aminophyllin three times a day and nitroglycerin tablets during attacks. The patient used only two of these during the next four years, but had taken six during the year before he was admitted.

In addition a herniorrhaphy had been performed seven years before admission, and a small cancer had been removed from the left cheek more than four years prior to entry.

Physical examination showed a well-developed and well-nourished man lying comfortably in bed. Numerous small licheniform areas were present on the chest and back. Examination of the heart and lungs was negative; the blood pressure was 130 systolic, 70 diastolic. The temporal, brachial and radial arteries were tortuous. There was tenderness in the entire right side of the abdomen, most marked in the right upper quadrant; the former point of maximum tenderness, indicated by the patient in the right lower quadrant, was not demonstrable at the time of examination. There was a hard, nodular, tender mass immediately to the right of the umbilicus. The left femur was 5 cm. shorter than the right, and the left trochanter was more prominent than the right. There was a slight compensatory scoliosis.

The temperature, pulse and respirations were normal.

Examination of the urine showed a + test for albumin, with 100 white blood cells per high-power field and many bacteria. Examination of the blood showed a red-cell count of 4,400,000 with a hemoglobin of 14.8 gm. (photoelectric-cell technic), and a white-cell count of 7900 with 69 per cent polymorphonuclears. The blood sugar was 79 mg. per 100 cc., and the nonprotein nitrogen of the blood serum 32 mg. A blood Hinton test was negative. A phenolsulfonephthalein test showed 5 per cent output of the dye the first fifteen minutes, and 55 per cent in one hour.

X-ray examination after a barium enema showed the tip of the cecum to be blunt, with a concave defect corresponding to the palpable mass. The barium given by mouth passed into the small bowel readily. The defect in the cecum reached the ileocecal valve but did not obstruct the lumen. One of the films revealed a pressure defect on the ileum about 3 cm. medial to the tip of the cecum, and on this film there was a suggestion that most of the mass was outside the cecum.

An electrocardiographic recording showed a normal rhythm and a rate of 65, with slight widening of the S waves in all leads and a slightly long PR interval — 0.20 second.

On the fifth hospital day the patient complained of a sudden severe pain that was dull in character and sharply localized over the xiphoid. The attack lasted for five minutes and then passed away completely. There were no accompanying symptoms, and a physical examination ten minutes later revealed no change in his condition. Two days later an exploratory laparotomy was performed.

DIFFERENTIAL DIAGNOSIS

DR. ARTHUR W. ALLEN: We have an elderly man who was admitted to the hospital with a mass in the right side of the abdomen that probably was of short duration. I say "probably," because he was in some department of the hospital two months prior to this entry, at which time they found pus in his urine but made no note of any mass in his abdomen. If it had been the same size and consistence that it was when the patient was admitted, they would doubtless have noticed it.

One should not worry too much about pus in the urine in a man of that age who had had a prostatectomy. I believe that this present illness does not have any bearing on the prostate operation or that it has anything to do with the urinary tract. The tenderness found in the right lower quadrant two weeks prior to entry is important. The record does not say whether the mass had increased in size between the time that tenderness was first noted and the time the patient was admitted to the hospital, but apparently in that two-week interval the location of the tenderness had changed from the right lower to the right upper quadrant. This complicates the picture.

I am not sure from the electrocardiographic tracings, whether the patient had coronary disease, but he had a history that would indicate such a disease; we know he had arteriosclerosis. Whether either of these conditions had any bearing on this picture, is very doubtful. I do not believe that this tender, palpable mass was an aneurysm. There is no evidence of its being expansile, and it came up rather too rapidly.

In a man of this age with a palpable mass in the abdomen, one invariably thinks first of cancer, and in this case it is a distinct possibility. A patient may have carcinoma of the cecum, with a large mass and subacute perforation, that has not been foreshadowed by any symptoms. It might reach this stage without giving us any more information than we have in this case. On the other hand, it is fairly unlikely. We should not expect a patient to be in such a perfect state of nutrition; furthermore, there is no mention in the hospital record of disturbances of the gastrointestinal tract so far as appetite is concerned, or any mention of change in bowel habits. Also opposed to the diagnosis of cancer is the fact that there was no anemia. I do not mean to imply that carcinoma of the cecum or ascending colon cannot be present with a very large mass without anemia. Although anemia is frequently present, it is not necessarily so.

A confusing feature in trying to interpret this as an inflammatory mass is the fact that the patient had an absolutely normal white-cell count, with a normal differential. This further complicates the picture.

Dr. James R. Lingley: As you see on these films, the barium enema reaches this point opposite the ileocecal valve, where it meets an obstruction. The tip of the cecum is not filled on any of the films, and no barium enters the terminal ileum. On this film, taken six hours after the motor meal, the terminal ileum is well filled, there is filling of the ascending colon, and the cecum again shows the same defect. The point that I am unable to decide is whether this defect so intimately associated with the tip of the cecum is caused by extrinsic pressure or by an intrinsic mass.

Dr. Allen: Can you see the kidney in the right side in any of these films?

Dr. Lingley: The kidney is pretty well obscured by the hepatic flexure, but I think it is in normal position and of normal shape.

Dr. Allen: Because of the patient's excellent condition, the lack of anemia and the lack of gastrointestinal-tract symptoms, I am going to hazard the guess that this is a subacute inflammatory process originating in the appendix, and that we are dealing with a subacute appendiceal abscess. I am making this diagnosis in the face of the normal white-cell count, which might have been highly elevated at some previous time in the earlier part of the illness. We have had four or five similar cases in which a mass in this region in elderly people has been interpreted as cancer and operated on under that diagnosis, the final diagnosis being that of an inflammatory process based on appendicitis. My second choice is cancer with subacute perforation, the lesion arising in the bowel in spite of the fact that the x-ray interpretation indicates that this was an extraluminal lesion. There are many other unusual situations that might explain this picture — mesenteric adenitis with a large mass outside of the bowel, or tuberculous lesion in the neighborhood of the ileocecal valve. We always must consider the possibility of lymphoma when dealing with any tender abdominal mass. These are possibilities that one ought to mention and consider, but my first choice is an inflammatory mass of appendiceal origin, and my second, cancer of the colon, with secondary inflammation around it.

Dr. Leland S. McKittrick: There was one point in the history which is a little different from that presented here, possibly because the patient did not know it — a mass was found by the urologist. The patient complained of a little soreness in his side, and a mass was felt at that time. That was what started the investigation that later led to his coming into the hospital and being examined. The X-ray Department said "probable carcinoma of the cecum." Operation was done with the diagnosis uncertain. We did not know whether he had carcinoma with a subacute process around it or a low-grade appendiceal abscess. One could not be sure of the best way to attack the problem. We elected to approach it as though it were a carcinoma. At operation the tumor mass was palpated with the greatest care, but no diag-

nosis could be made. The liver was free from metastases. I thought that the mass, as I felt it from within the abdomen, was probably malignant. He had an ileotransverse colostomy done as the first step of a two-stage direct approach to the tumor mass at a later time.

Dr. Tracy B. Mallory: I take it that the subsequent course was never good enough to make any further operation possible?

Dr. McKittrick: No; the subsequent course was such that the second "operation" was done by Dr. Mallory. The patient's immediate response to operation was perfectly satisfactory. However, he then ran an unexplained fever. We were confident that he did not have peritonitis. On the other hand he had more tenderness in the right flank than he had had previously, but even that did not wholly satisfy the clinical picture which he presented. He developed cerebral symptoms and died, I have forgotten how many days after operation; it was a death that we could not satisfactorily explain. We did think that there had been extension of the infection in the right flank. We could not quite see how that was responsible for the course that he ran, but we believed that he did not have general peritonitis. The ileotransverse colostomy was functioning satisfactorily.

Preoperative Diagnosis

Carcinoma of the cecum.

Dr. Allen's Diagnosis

Subacute appendicitis, with abscess formation?
Carcinoma of the colon, with subacute perforation?

Anatomical Diagnoses

Appendiceal abscess.
Brain abscess, right frontal area.
Pulmonary congestion and edema.
Cholecystitis, chronic.
Cholelithiasis.
Cholesterosis of gall bladder.
Cardiac hypertrophy, hypertensive type.
Operative wound: left rectus incision for ileotransverse colostomy.
Arteriosclerosis, coronary and aortic.
Hydrothorax, bilateral.

Pathological Discussion

Dr. Mallory: At autopsy 700 cc. of slightly turbid fluid was found in the peritoneal cavity; there was a very large firm mass that was evidently mostly omentum. On breaking into it, a central abscess cavity containing 60 cc. of pus was found, and in its midst was the stump of the appendix. The actual cause of death, however, was not the peritoneal sepsis. It was a metastatic abscess of considerable size in the right frontal lobe of the brain. There was evidence of chronic cholecystitis, and a few small stones were present in the gall bladder, but there was no evidence that this infection played any part in the fatal outcome. The coronary arteries showed only slight atheroma, and there were no scars of myocardial infarction. There was, however, moderate hypertrophy of the hypertensive type.

Dr. Allen: I think that the proper operation was done for this particular patient. If you break into such a mass thinking it is an appendiceal abscess and find it to be carcinoma, you have robbed the patient of some of his chances of having a successful extirpation of the tumor. I think one might well argue that had the abscess been drained at the first operation he might have been spared the metastatic abscess later on, but this does not necessarily follow. He could have had a brain abscess after drainage of the appendiceal abscess. I am sure that if I had had this problem I should have handled it exactly as Dr. McKittrick did, that is, with a two-stage operation.

Dr. McKittrick: Dr. Allen has suggested the difficulty, at operation, of differentiating cancer of the cecum and an appendiceal abscess. It is of interest in this connection that after the pathologist had removed the abdominal contents and arranged them on the table, he made a diagnosis of cancer. Not until he had broken through the abscess and into the cecum could he be sure there was no cancer.

CASE 26432

Presentation of Case

A sixty-three-year-old woman entered the hospital complaining of difficulty in breathing of five weeks' duration.

The patient stated that at the age of twenty-eight she had been a victim of a milk-borne streptococcal infection in which all her joints became red and swollen, and that during this time an aortic valvular lesion was discovered. She lived a normal active life until one year before admission, when she began to suffer from breathlessness, anorexia and loss of weight. The dyspnea was marked at the beginning of this period, but improved and did not return in all its severity until five weeks before admission, although she had had occasional attacks of nocturnal dyspnea. In addition she had noticed swelling of her ankles. Two days before admission the patient developed an unproductive cough and hoarseness.

The past illnesses and family history were irrelevant.

Physical examination showed a well-developed but poorly nourished woman, who appeared chronically ill and lay propped up in bed breathing quietly. The neck veins were distended to about 5 cm. above the sternum. The heart was moderately enlarged to the left, and a systolic thrill was palpable at the base. A harsh systolic murmur was heard in the aortic area, with a diminished aortic second sound; the sounds were of poor quality, with a gallop rhythm. The blood pressure was 120 systolic, 75 diastolic. At the lung bases the percussion note was dull, the tactile fremitus and breath sounds were diminished and a few moist rales were heard. There was pitting edema of the legs to the knees.

The temperature and respirations were normal, and the pulse varied between 80 and 120.

Examination of the urine showed a + test for albumin, with 30 white blood cells per high-power field, and many unidentified bacteria. The blood showed a red-cell count of 4,760,000 with a hemoglobin of 11.5 gm. (photoelectric-cell technic), and a white-cell count of 12,100. The nonprotein nitrogen of the blood was 42 mg. per 100 cc. A blood Hinton test was negative.

Four days after admission the patient complained of severe "gas pains" in the right upper quadrant that radiated to the back to a point immediately below the scapula. Examination at that time revealed an enlarged very tender liver. In general the patient's course was progressively downhill, although treatment improved the peripheral edema. In the last few days of her illness she became disorientated and developed a decubitus ulcer of the sacrum. The patient died two months after admission.

Differential Diagnosis

Dr. Edward F. Bland: This is a fairly clear-cut story, and the physical signs are well described in so far as the structural lesion is concerned. Perhaps we should consider this aspect of the case before discussing the question of etiology. It seems reasonably clear that there was aortic stenosis of considerable degree. All the physical signs are consistent with that diagnosis, namely, a harsh, basal systolic murmur maximal to the right of the sternum and accompanied by a systolic thrill and by diminution in the intensity of the second sound. To make the picture complete we might like a narrow pulse pressure, but we need not be disturbed by its absence, since some patients with well-marked aortic stenosis may even have hypertension. About half the patients with aortic stenosis also have a very slight degree of aortic regurgitation, manifested by a faint diastolic murmur along the left border of the sternum. It seems remarkable that all of them do not have a slight degree of aortic regurgitation. A fair number of patients with well-marked aortic stenosis also have evidence of other valvular disease, especially of the mitral valve, but from this record we have no indication of such disease. Finally, the clinical course that this patient ran is characteristic of well-marked aortic stenosis, possibly calcific in type.

Next we must consider the etiology. I hesitate somewhat to reopen that question again. The cause of this lesion has been the source of much discussion and considerable disagreement among capable observers. I think most people agree that aortic stenosis is superimposed either on previous inflammatory lesions in the valve cusps or in that vicinity, or less often on a congenital defect, usually a bicuspid aortic valve. The latter, of course, is relatively rare. There has been a tendency among pathologists to relinquish previously held ideas concerning the possible role of Mönckeberg's sclerosis in some of the otherwise unexplained cases. Finally, as regards etiology, a few years ago it was suggested that in an occasional case of well-marked aortic stenosis, the preceding inflammatory change in the valve might perhaps have been due to a mild subacute bacterial endocarditis from which the patient was fortunate enough to recover. There is not really much evidence to favor this point of view. From the clinical standpoint a history of rheumatic fever or chorea is obtained in one third to one half of this group of patients. In a considerable additional number, bringing the total up to about 75 per cent, there is a past history of unusually frequent sore throats and respiratory infections. From the pathological point of view, I am of the opinion that Dr. Louis Gross before he died was inclined to think that the majority represented superimposed calcification on old rheumatic damage of the valve. At a meeting last year in Pittsburgh, Dr. Ernest Hall suggested that perhaps all or at least a very high percentage were of this origin. The belief in the pathology department of this hospital is that a considerable number, perhaps not all, are the result of healed rheumatic inflammation in the valve.

The incidence of this condition is of some interest. In this hospital it is noted about twice in a hundred postmortem examinations, and as one sees cardiovascular patients, about three in a hundred have physical signs of this lesion. It is also true that it is commoner in the northern states than in the South, where infections in general, and rheumatic

infection in particular, are somewhat less common.

The clinical features have been well described by numerous observers, and this patient's course is fairly characteristic. The valve lesion is usually well tolerated for many years, but when cardiac failure finally ensues, the heart fails to respond satisfactorily to digitalis and diuretics. We are not told much about the therapy of this case, but we can assume that the patient had received rest, digitalis and diuretics. The course, however, was progressively downhill, as we should expect. It is also true that many of these patients have angina pectoris, but I could identify nothing in this record as angina pectoris. Many of these patients have spells of dizziness and faintness, and sudden death is not uncommon with well-marked aortic stenosis. Relatively few develop subacute bacterial endocarditis. Auricular fibrillation, which I assume was not present in this case, is relatively rare except in those patients in whom aortic stenosis is associated with rheumatic disease of the mitral valve.

There are two questions we might like to raise, but I do not know whether the information would be particularly helpful. First, nothing is said about this patient's electrocardiogram. We should expect that, if characteristic, it would show some degree of left-axis deviation. Intraventricular block is not so uncommon as auriculoventricular block. Abnormal T waves are almost the rule. Finally I am curious to know what the x-ray examination revealed in this patient, because in our experience here approximately 75 to 80 per cent have calcium deposits superimposed on the valvular lesion. The more interested we have become in this condition, the oftener we have been able to detect the calcium under the fluoroscope. It is more easily shown under the fluoroscope than in films, even with films taken with a special technic to demonstrate it. Another point in relation to the x-ray findings that might be of interest is the contour of the left auricle. Although there were no physical signs suggesting involvement of the mitral valve, it would have been interesting to confirm this by careful study of the left auricle under the fluoroscope.

One is left, then, with not much choice as to diagnosis. One other condition might be mentioned in passing. I know of three or four younger people with congenital subaortic stenosis who are in good health. I suppose some time or other we may see this condition in an older person, since it causes relatively little strain on the heart. I suspect that this was not the answer here. I will make a diagnosis of aortic stenosis, probably calcific, with congestive heart failure.

Dr. Howard B. Sprague: I can answer a few of the questions that Dr. Bland asks. I saw this woman first in January, 1939, when she began to have attacks of cardiac asthma, but her previous story included a year of very definite angina pectoris on exertion and a burning sensation under the sternum that was relieved by rest. The cardiac asthma started abruptly and disturbed her every night. At that time she showed evidence of aortic stenosis and an aortic diastolic murmur. The blood pressure when she was first seen was 180 systolic, 105 diastolic. There were a few rales at the lung bases and some sacral edema. She was digitalized at that time, with complete relief of the symptoms for several months. In fact, I did not see her again for over a year, and then she gave a story of having had only three attacks in the intervening period; she had, however, been very much limited in activity on account of dyspnea and substernal oppression. She had become very depressed because she had had to change abruptly from being a very active woman to one who was partly bedridden. She then showed pulsus alternans and increasing congestive failure, and was admitted to the hospital for mercurial therapy. I should add that after I saw her at home she came to the office, where definite calcific aortic stenosis, without evidence of mitral disease, could be demonstrated under the fluoroscope.

Dr. Bland: In view of the history of angina pectoris mentioned by Dr. Sprague, may I ask him if he expects to find the coronary arteries in good or poor condition?

Dr. Sprague: It would not be fair for me to answer that, since I know what the autopsy showed.

Dr. Paul D. White: I saw the patient with Dr. Sprague and thought that she had a very high degree of aortic stenosis; it is surprising that she lived as long as she did with the signs that showed on physical examination.

Clinical Diagnoses

Rheumatic heart disease, old.
Calcific aortic stenosis.
Decubitus ulcer.

Dr. Bland's Diagnoses

Aortic stenosis, probably calcific.
Congestive heart failure.

Anatomical Diagnoses

Aortic stenosis, calcareous.
Pulmonary infarcts, multiple, old and recent.
Thrombosis, right popliteal vein, antemortem.

Cardiac hypertrophy, hypertensive type.
Nephritis, chronic vascular.
Hydrothorax, bilateral.
Chronic passive congestion of liver, slight.
Pulmonary edema, slight.
Peripheral edema, slight.
Arteriosclerosis, coronary and aortic, slight.
Decubitus ulcer.

Pathological Discussion

Dr. Tracy B. Mallory: The postmortem examination showed calcific aortic stenosis of a very severe grade. The valve, when one looked down on it from above, showed a slit-like opening between two cusps that were almost of equal size, although one was slightly larger than the other. Both sinuses of Valsalva were completely filled with irregular nodules of very hard calcified material. There can be no question that there was an underlying bicuspid aortic valve. In a bicuspid valve the two valves are never quite of equal size; the two fused cusps, however, measure somewhat less than the sum of two normal cusps, and the remaining cusp is always greater than any single normal cusp would be, and that was very clearly evidenced here. In many cases it is quite impossible to decide grossly whether a bicuspid valve underlies the lesion. My personal impression would be to disagree with Dr. Bland and think that very often a bicuspid valve underlies this condition. However, members of my own department do not always agree with me, and you can therefore see that it is an unsettled question. It is possible histologically to distinguish bicuspid valves with reasonable certainty by studying the relation of the various layers of the aortic wall to each other at the point of commissure. That can easily be done when there is no calcification, but in a case like this, decalcification is so difficult and takes so long that it is ordinarily impossible to stain the wall successfully; most of our efforts have been very disappointing, and that has been the experience of almost everyone else. The coronary arteries showed moderate but not severe atheroma without narrowing. There was no thrombosis. The mitral valve was grossly normal.

A surprising finding at autopsy that was not foreshadowed, so far as I can see, by anything in the clinical story was a number of quite large pulmonary infarcts — four good-sized ones, three of which had evidently been present for a long time. One was fairly fresh and may have occurred during the stay in the hospital, and the others certainly antedated admission. It is not impossible that the final episode of failure may have followed infarction, although we have no clear evidence of that. Usually with pulmonary infarction one can count on a significant rise in temperature, but even that was absent in this case. The temperature did not go above 99.2°F. at any time in the hospital, probably because the majority of the infarcts occurred and the febrile reaction was over before the patient was admitted. As regards the etiology, Dr. Bland has already outlined the argument, and I can only say that this case is one that I can regard as exceptional because it had a clear-cut history of rheumatic fever, which very few of the cases show, and a grossly negative mitral valve.

Dr. White: How big was the heart?

Dr. Mallory: It weighed 650 gm.

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MEDICAL EDUCATION IN THE UNITED STATES

MEDICAL education always has been a baffling affair to many people: to students who must be educated, to teachers who must educate, and to doctors who must practice. Thus, the topic of medical education has been thrashed out all over New England since at least 1782, and there still is grave doubt in the minds of those interested in the problem as to whether there yet is any certain formula to describe the best way of managing so complex a contrivance.

In 1933 the Council on Medical Education and Hospitals of the American Medical Association voted to undertake a comprehensive re-survey of the medical schools of the United States and Canada. The final result was recently printed in the form of an extensive report.*

*Committee on Medical Education and Hospitals: *Medical Education in the United States, 1934–1939*. 249 pp. Chicago: American Medical Association, 1940.

This report is full of interesting data and is worth careful study. It has been written skilfully; instead of describing individual schools and making comparisons that might well be invidious, the book deals with broader views: the aims and policies of American medical education, differences in the programs of organization and administration in different schools and trends in medical education.

As in every comparative analysis of an imponderable substance like quality, among medical schools, too, it appears that there are many that are good, some that are better, and some that are still better. Underlying medical education in all schools, however, are two peculiarities that are worth noticing.

Medical education today is expensive, — from two to seven times more expensive than any other form of professional education, — and this is chiefly the result of its being so time-consuming. Nowadays more than half the medical students experience four or more years of college study before they begin the study of medicine. Thirteen of the schools require a year of internship after four years of medical-school training before their students may receive their degrees. Specialty practice has become popular, and adequate preparation for any of its forms appears to require intensive training for a considerable period of time after a man has been through medical school and hospital. All this may be sound, but it greatly increases the cost of medical education. The schools with greatest wealth are likely to attract the most active teachers and to offer their students the best facilities for study and inspiration. There is indeed a strong responsibility for leadership in medical research and teaching resting in the hands of those medical schools that have been fortunate enough to have obtained large endowments.

The recent popularity in specialism has tended to shift the teaching of the specialties out of the medical school. This is satisfactory to the student who can afford to acquire training in a specialty but not so helpful to the one who must set up his shingle in general practice as soon as he can. It is said that some have had teaching in the specialties so neglected in their undergraduate days

that when they were on their own they found themselves unable to make a complete examination of a patient. And this seems scarcely the best way to improve the average of ordinary work.

On the whole, however, the present health of medical education in the United States is in a vastly more vigorous state than it was in 1910 when Abraham Flexner's report appeared. Bad schools have been deleted, good schools have been strengthened, the general level of teaching has been raised, and doctors are better and more intelligently trained than they were a generation ago. Medical education is by no means perfect. But what system of education is?

ONE PROBLEM IN THE DIAGNOSIS OF CANCER

One of the aspects of the cancer problem that makes diagnosis difficult is the infrequency of cancer cases in relation to the general type of patient coming to the practitioner's office, as well as the tendency to a concentration of cancer cases, through one means or another, so that many practitioners see very few. In Massachusetts, a physician might expect to see two to three cancer patients a year if the cases were evenly distributed. The effect of concentration is not definitely known, but undoubtedly patients who suspect that they have cancer go to men who have established a reputation for special interest or competence in that field.

A recent paper by McDowell* of the United States Public Health Service gives the results of a study of this problem in the Pittsburgh area. On the basis of case records and death certificates, there were, in the year 1937, 6103 cases of cancer under medical care or certified as dying from cancer. Strikingly enough, over 50 per cent of these cases were reported by 0.3 per cent of the doctors and 16 per cent of the hospitals. Nearly half the doctors and half the hospitals reported no cases of cancer during this period. The need for intensive cancer education in this area is shown by the fact that 59 per cent of fatal cases had been diagnosed as malignant less than six months before death, and 80 per cent of them less than a year. This means a long period of delay in the vast majority of cases.

If the experience in Massachusetts can be trusted the only way to cut down this delay period is through intensive educational effort among the laity, guided by and with the co-operation of physicians.

*McDowell, A. J.: The incidence of cancer in Pittsburgh and Allegheny County, Pennsylvania, 1937. *Pub. Health Rep.* 55:1419-1451, 1940.

OBITUARY

HENRY JACKSON

1858–1940

Henry Jackson died on October 4, 1940, in his eighty-second year. So is another taken from the fast-thinning ranks of those physicians who practiced the art of medicine and at the same time helped materially to lay the solid foundations upon which our science of today is built. His life epitomized the ideal family doctor.

All who had contact with Dr. Jackson, whether patient, friend or young student of medicine, adored him. What formal teaching he did was at the Boston City Hospital in connection with the Harvard Medical School. His students and more especially his house-officers never tire, even to this day, of quoting "Uncle Henry" and never fail, whenever they get beyond their depth, to fall back on his sound common sense and never-to-be-forgotten aphorisms. Informally he taught much sound medicine to many, — usually by precept and example, — and until his retirement he was constantly searching for new roads to perfection — as witness his own early use of the McKenzie polygraph in the study of heart disease. But above all, he taught a generation of students to look on patients as human beings and to regard their diseases in the light of their personal idiosyncrasies.

He had, to be sure, his own lovable peculiarities, which only endeared him the more to his friends and patients. No one who really knew him could imagine Dr. Jackson leaving his house without his famous square-topped hat. His presence in the home was always cheerfully announced from just inside the front door no matter if the family were three stories up, and even the sick-

est patient's morale rose promptly in response. He could do anything with children of all ages, and was as fond of them as they were of him. When he was on service at the Boston City Hospital, he invariably carried a pocketful of bright new pennies and solemnly presented one to each sick child every day. A logician and purist in all things, he insisted on kindly efficiency, self-respecting industry, unvarnished truth and consideration for others in all about him, and set the example by imposing the same standards on himself. In the days when thyroid disease and so-called "sciatica" were much in the medical eye, he was just as insistent in refusing to Anglicize the French word *goitre* as he was in condemning the inadequacy of a wastebasket diagnosis such as sciatica.

He had a great sense of personal dignity and demanded and received the respect due him. In return he expected all those about him to show the same attributes, and he was the first to accord them due respect. He abhored all sham and dishonesty under any guise. He had a sharp tongue and could, on occasion, put it to good use. He was far quicker to praise than to blame and saw to it that credit was given where credit was deserved.

After his retirement, his physical and mental activities were unabated, and he continued to find intellectual outlets for his many energies, among them the study of conversational French and French literature. During the last years of his life he was practically blind, yet he continued to visit his many friends — and they came from all walks of life — and to keep in touch with his old students.

He was able to go to North Haven, Maine, for this, his last, summer, and although his activities were much restricted he could still sail in his beloved Penobscot waters, as he had for nearly fifty years. It is said that his boatman, on being told that Dr. Jackson was ill and could not sail with him that day and probably never would be able to do so again, retorted, "I know better; the trouble with Dr. Jackson is that he ate too many chocolates yesterday." He did indeed partly recover his health, but was forced shortly to leave North Haven and return to Chestnut Hill, where he died peacefully after another short illness. As Oliver Wendell Holmes said of James Jackson, so it may be said of his nephew, Henry, "He was a child to learn, a father to teach, a brother to help."

> Honour the physician for the need thou hast of him; for the most High hath created him.

MEDICAL EPONYM

S Curve of Ellis

At a meeting of the Boston Society for Medical Improvement, October 13, 1873, Professor Calvin Ellis (1826–1883), of the Harvard Medical School, discussed "The Line of Dulness in Pleuritic Effusion." His remarks were reported in the *Boston Medical and Surgical Journal* (**90**:13, 1874).

> But, in a certain number of cases where the effusion is quite large, if an accurate line be drawn, the flatness will be found to describe a curve, gradually approaching the spine toward the base of the chest, having a space from one to three or more inches broad between the spine and the line of flatness. In this space, resonance will still be detected, and respiration heard. As the effusion increases, this line approaches nearer and nearer the spine, until the whole back becomes flat.

The attention of Ellis was called to the fact that Damoiseau had described a similar curve in "Recherches cliniques sur plusieurs points du diagnostic des épanchements pleurétiques" which was published in *Archives générales de médecine* (Series 4, **3**:129–156, 1843). He said that until his attention had been called to this, he had not been aware that the point had been observed but that Damoiseau's description of this curve agreed with his observation.

An article by Ellis, entitled "The Curved Line of Pleuritic Effusion," appeared in the *Boston Medical and Surgical Journal* (**95**:689–697, 1876). It consists of a series of case histories and several diagrams showing a curve on the posterior aspect of the thorax in the form of an S whose tail begins at the vertebral column and whose tip descends into the axilla toward the sternum. The text contains no description of the term, the "S curve of Ellis," which was applied by Garland on pages 6 and 16 of *Pneumono-dynamics* (New York: Hurd and Houghton, 1878).

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

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330 Dartmouth Street
Boston

Diabetes Resulting in Intrauterine Death of the Fetus

Mrs. M. H., a thirty-five-year-old para III, was first seen in the office on July 5, 1929. At that time she was four and a half months pregnant.

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

The family history was non-contributory. The patient's diabetes was discovered during her second pregnancy in 1924, and three days after its discovery the patient went into diabetic coma. This pregnancy was terminated at seven months, with a stillborn child. The first pregnancy in 1922 was full term, but the baby died. Catamenia began at thirteen, were regular with a twenty-eight-day cycle and lasted three days with no discomfort. The last regular period was February 15, making the expected date of confinement November 22, 1929.

Physical examination at the time of her first visit showed a well-developed and well-nourished woman. The weight was 120 pounds. The heart was not enlarged; there were no murmurs. The lungs were clear and resonant; there were no rales. The blood pressure was 120 systolic, 66 diastolic. Vaginal examination revealed a relaxed perineum and the fundus at a level consistent with her dates. The urine contained 1.5 per cent sugar. Under the direction of a specialist in diabetes, the patient was taking 18 units of insulin daily; this dosage was later increased to 34 units.

The patient was seen frequently by both the obstetrician and the consultant, and routine samples of blood for determining the sugar concentration were taken at each visit; the lowest level was 109 mg. per 100 cc., on August 23, and the highest, 200 mg., on October 25.

On November 7 the patient seemed in good condition. The weight was 132 pounds. The blood sugar was 140 mg. per 100 cc., and the urine contained 1.1 per cent sugar. The blood pressure was 120 systolic, 70 diastolic. Abdominal examination revealed the vertex presenting, and the fetal heart was heard. On vaginal examination the cervix was soft, not open but somewhat taken up. The uterus seemed to have shrunk, although the baby had grown.

The patient entered the hospital on November 14 for better control of the diabetes. On November 15 the fetal heart was not audible. On November 19 the patient weighed 122 pounds, a loss of 10 pounds since November 7. She remained in the hospital until December 5, when labor started spontaneously. A large macerated fetus was delivered normally, although there was considerable difficulty with the shoulders. The placenta was very small, in contrast to the very large placentas which are seen in many diabetic patients.

The patient was seen in the office on January 13, 1930, for a final examination. At that time the urine had been sugar-free for five days, and she felt very well. The weight was 116 pounds. Pelvic examination was negative.

There have been no further pregnancies.

Comment. Intrauterine death in the last few weeks of pregnancy is one of the hazards of a pregnancy complicated by diabetes, even when treated with insulin. The loss of weight of 10 pounds between November 7 and November 19 shows that the patient must have been quite edematous. The actual weight of the fetus is not in the hospital record, but inasmuch as there was considerable difficulty with the shoulders, it is fair to infer that it was a large one. The previous obstetric history surely warranted earlier delivery when it was known that the baby was alive, and the size of the baby thoroughly justified the assumption that ten days before its death the baby would have weighed enough to ensure its viability.

Experience has shown that at approximately thirty-six weeks diabetic patients should be sent to the hospital in order to be under daily supervision, unless complications demand an earlier entry.

This case illustrates the intelligent conservative treatment of a known intrauterine fatality. When the uterus harbors a dead fetus, it is wiser to leave it alone than to attempt the induction of labor.

POSTGRADUATE EXTENSION COURSES

The following sessions, given by the Massachusetts Medical Society in co-operation with the Massachusetts Department of Public Health, the United States Public Health Service and the Federal Children's Bureau, have been arranged for the week beginning October 28:

BARNSTABLE

Sunday, November 3, at 4:00 p.m., at the Cape Cod Hospital, Hyannis. Dermatitis and Eczema. Instructor: John G. Downing. Donald E. Higgins, *Chairman.*

BRISTOL NORTH

Thursday, October 31, at 4:00 p.m., at the Morton Hospital, Taunton. Obstetric Complications: With case histories and clinical problems. Instructor: Christopher J. Duncan. Lester E. Butler, *Chairman.*

BRISTOL SOUTH (New Bedford Section)

Friday, November 1, at 4:00 p.m., at St. Luke's Hospital, New Bedford. Diagnosis and Treatment of Minor Lesions of Rectum and Anus. Instructor: Neil W. Swinton. Robert H. Goodwin, *Chairman.*

ESSEX NORTH

Friday, November 1, at 4:30 p.m., at the Clover Hill Hospital, Lawrence. Dermatitis and Eczema. Instructor: J. Harper Blaisdell. John Parr, *Chairman.*

ESSEX SOUTH

Tuesday, October 29, at 4:00 p.m., in the Conference Room, Salem Hospital, Salem. Pediatric Case Discussions. Instructor: James M. Baty. J. Robert Shaughnessy, *Chairman*.

MIDDLESEX NORTH

Friday, November 1, at 5:00 p.m., at St. John's Hospital, Lowell. Chemotherapy in the Treatment of Gonococcal Infection. Instructor: Sylvester B. Kelley. William S. Lawler, *Chairman*.

PLYMOUTH

Tuesday, October 29, at 4:30 p.m., in the Nurses' Home of the Brockton Hospital, Brockton. The Treatment of Varicose Veins. Instructor: E. Everett O'Neil. Walter H. Pulsifer, *Chairman*.

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University of Breslau and Berlin, 1925.

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COLE, RALPH E., Westford.
Tufts College Medical School, 1938.

D'ARTUN, BARON A., 105 Westford Street, Lowell.
Faculty of Medicine in Lausanne, 1919.

LANDAU, IRVING I., Boston Road, Pinehurst.
University of Berlin, 1934.

LEWIS, ELIZABETH K., Main Street, Groton.
Tufts College Medical School, 1937.

LEWIS, F. WOODWARD, Main Street, Groton.
Tufts College Medical School, 1937.

SVIBERGSON, NILS E., Tewksbury State Hospital, Tewksbury.
Tufts College Medical School, 1936.

THOMAS, EDWIN B., Tewksbury State Hospital, Tewksbury.
Tufts College Medical School, 1938.

Raoul L. Drapeau, *Secretary.*

MIDDLESEX SOUTH DISTRICT

BLOOMENTHAL, ABRAHAM P., 5 Bank Street, Waltham.
Middlesex University School of Medicine, 1934.

BOWEN, DONALD E., 42 Parsons Street, West Newton.
Tufts College Medical School, 1939.

BURGER, FRANCIS J., JR., 148 North Beacon Street, Watertown.
Middlesex University School of Medicine, 1930.

BURKE, EDWARD W., 17 Rose Garden Circle, Brighton.
Tufts College Medical School, 1935.

BOYER, NORMAN H., 1932 Massachusetts Avenue, Lexington.
Tufts College Medical School, 1934.

CAMPBELL, HARRY L., 639 Fellsway West, Medford.
Boston University School of Medicine, 1938.

CHASE, WINNIFRED P., 385 High Street, West Medford.
Tufts College Medical School, 1934.

DROSDIK, VINCENT A., 503 Main Street, Watertown.
Middlesex University School of Medicine, 1926.

EDSALL, GEOFFREY, 36 Follen Street, Cambridge.
Harvard Medical School, 1934.

FORZIATI, ANTHONY A., 113 Ferry Street, Everett.
Middlesex University School of Medicine, 1932.

FOSTER, FRANK P., 31 Magnolia Avenue, Newton.
McGill University Faculty of Medicine, 1933.

HALL, VOLTA R., JR., 163 Hillside Avenue, Arlington Heights.
Western Reserve University School of Medicine, 1934.

HOWARD, PAUL M., McLean Hospital, Waverley.
University of Pennsylvania School of Medicine, 1933.

JOHNSON, DANIEL P., 8 Quincy Street, Watertown.
University of Lausanne, 1937.

KEMPF, GROVER A., United States Marine Hospital, Brighton.
Indiana University School of Medicine, 1910.

LEPORE, JOHN J., 69 Essex Street, Marlboro.
Georgetown University School of Medicine, 1937.

LOWENTHAL, KARL, 45 Englewood Avenue, Brighton.
University of Freiburg, 1915.

MASTRANGELO, LOUIS, 572 Mt. Auburn Street, Watertown.
Middlesex University School of Medicine, 1930.

McKITTRICK, JOHN B., 60 Greenwood Avenue, West Newton.
Harvard Medical School, 1937.

MUELLER, HANS P., 9A Ware Street, Cambridge.
Medical School of University of Koenigsberg, 1931.

NAUEN, ALICE B., 142 Sutherland Road, Brighton.
University of Hamburg, 1926.

POLLEN, DAVID A., 17 Radcliffe Road, Allston.
Middlesex University School of Medicine, 1932.

ROSS, RALPH A., 42 Englewood Avenue, Brighton.
Harvard Medical School, 1935.

SEGEL, ARNOLD L., 1959 Commonwealth Avenue, Brighton.
Harvard Medical School, 1936.

STENZEL, FRANZ R., 1580 Beacon Street, Waban.
Harvard Medical School, 1938.

SPRAGUE, JOHN S., 75 Nottinghill Road, Brighton.
Johns Hopkins University School of Medicine, 1936.

YOUNG, DAVID A., McLean Hospital, Waverley.
Harvard Medical School, 1931.

Alexander A. Levi, *Secretary*.

NORFOLK DISTRICT

ADAMS, EDWARD E., 4121 Washington Street, Roslindale.
Boston University School of Medicine, 1937.

ALLEN, EDWARD C., 26 Aspinwall Avenue, Brookline.
Tufts College Medical School, 1939.

CRAGG, GRACE T. M., Medfield State Hospital, Harding.
Dalhousie University Faculty of Medicine, 1922.

DE AGUIAR, ALCINDA P., Wrentham State School, Wrentham.
Oporto University, Portugal, 1925.

ELSBERG, ALBERT, 57 Thorndike Street, Brookline.
University of Berlin, 1913.

FAILLACE, FEDELE M., 44 Penniman Road, Brookline.
Royal University of Rome, 1934.

FERGUSON, ALBERT B., 1080 Beacon Street, Brookline.
Cornell University Medical College, 1917.

FRIEND, DALE G., 2 Autumn Street, Boston (Roxbury).
Harvard Medical School, 1935.

GROSSMAN, SAMUEL, 32 Wenonah Street, Roxbury.
Kansas City University of Physicians and Surgeons, 1932.

HEAVEY, THOMAS J., 4 Broad Street, Medway.
Middlesex University School of Medicine, 1922.

HOCHMAN, GEORGE V., 20 Harding Street, Sharon.
Middlesex University School of Medicine, 1934.

HOERR, STANLEY O., 159 Kent Street, Brookline.
Harvard Medical School, 1936.

HOOVER, HAROLD R., 721 Huntington Avenue, Roxbury.
University of Southern California School of Medicine, 1937.

KARPATI, OSCAR, 1477 Beacon Street, Brookline.
Royal Hungarian State "Elizabeth" University, Pecs, Hungary, 1926.

LARSON, CARROLL B., 60 Egmont Street, Brookline.
State University of Iowa College of Medicine, 1933.

LENDGREN, CARL V., 69 Central Street, Foxboro.
Boston University School of Medicine, 1930.

LOWIS, SAMUEL, 114 University Road, Brookline.
Harvard Medical School, 1934.

MILLER, WALLACE C., Peter Bent Brigham Hospital, Roxbury.
Loyola University School of Medicine, 1936.

PERONA, ATTILIO C., 12 Linden Street, Norwood.
Middlesex University School of Medicine, 1934.

PIKE, GEORGE M., 368 Longwood Avenue, Roxbury.
Harvard Medical School, 1936.

PORAS, HARRY H., 208 Rawson Road, Brookline.
University of Vienna, 1929.

PROVENZANO, ROSARIO W., 62 Adams Street, Dorchester.
Tufts College Medical School, 1940.

ROTHBLATT, BERNARD W., 26 May Street, Jamaica Plain.
Tufts College Medical School, 1937.

SCHIRMER, ADELBERT F., 172 Kittredge Street, Roslindale.
Tufts College Medical School, 1939.

SCHULZ, MILFORD D., 6 Autumn Street, Boston (Roxbury).
Northwestern University Medical School, 1936.

SEALE, EARL S., 116 Riverway, Boston (Roxbury).
Tulane University of Louisiana School of Medicine, 1935.

SHWACHMAN, HARRY, 62 Elm Hill Avenue, Roxbury.
Johns Hopkins University School of Medicine, 1936.

STEAD, EUGENE A., JR., Peter Bent Brigham Hospital, Boston (Roxbury).
Emory University School of Medicine, 1932.

STONE, NATHANIEL M., 94 Naples Road, Brookline.
Tufts College Medical School, 1937.

WEATHERLY, HOWARD E., 20 Netherlands Road, Brookline.
State University of Iowa College of Medicine, 1934.

WELCH, RICHARD F., 108 Brook Road, Milton.
Middlesex University School of Medicine, 1935.

YEOMANS, ANDREW, 38 Webster Place, Brookline.
Harvard Medical School, 1935.

YOUNG, ALEXANDER, 1110 River Street, Hyde Park.
Middlesex University School of Medicine, 1934.

Frank S. Cruickshank, *Secretary*.

NORFOLK SOUTH DISTRICT

FRANKMAN, WILLIAM, 736 Hancock Street, Wollaston.
St. Louis College of Physicians and Surgeons, 1921.

MILLEN, MORRIS H., 391 Bridge Street, North Weymouth.
Middlesex University School of Medicine, 1933.

PEARLSTEIN, MAX, 447 Washington Street, Braintree.
Tufts College Medical School, 1929.

SAWYER, JOSEPH H., 1 Monatiquot Avenue, Braintree.
Massachusetts College of Osteopathy, 1927.
Middlesex University School of Medicine, 1931.

SLOANE, WILLIAM C., 15 South Main Street, Randolph.
Middlesex University School of Medicine, 1934.

WILLIAMS, ROBERT H., 56 Sycamore Road, Squantum.
Johns Hopkins University School of Medicine, 1934.

Henry H. A. Blyth, *Secretary*.

PLYMOUTH DISTRICT

GOETZE, SIEGBERT, 815 Washington Street, Stoughton.
University of Freiburg, 1909.

MCGEE, CHARLES J., 118 Hillcrest Avenue, Brockton.
Harvard Medical School, 1937.

VOGEL, FRIEDRICH, Camp Pembroke, Pembroke.
University of Vienna, 1924.

WASSERSUG, JOSEPH D., Lakeville.
Tufts College Medical School, 1938.

Ralph C. McLeod, *Secretary.*

SUFFOLK DISTRICT

ASSAD, FREDERICK C., One Bond Street, Boston.
Middlesex University School of Medicine, 1934.

CHISHOLM, JULIAN F., JR., 17 Pinckney Street, Boston.
Johns Hopkins University School of Medicine, 1930.

COHEN, MORRIS A., 452 Beacon Street, Boston.
College of Physicians and Surgeons, Boston, 1919.

DEMING, JULIA, 406 Marlboro Street, Boston.
Woman's Medical College of Pennsylvania, 1922.

DENHOFF, ERIC, Boston City Hospital, Boston.
University of Vermont College of Medicine, 1938.

DIAMOND, MORRIS, c/o Lieberman, 10 Mulberry Road, Larchmont, New York.
University of Vienna, 1920.

FARRINGTON, ROBERT F., Boston City Hospital, Boston.
Harvard Medical School, 1940.

FELL, ERNEST M., 202 West Newton Street, Boston.
Tufts College Medical School, 1939.

HIRSCH, OSKAR, 400 Commonwealth Avenue, Boston.
University of Vienna, 1902.

HUNTINGTON, BENJAMIN L., 311 Marlboro Street, Boston.
Harvard Medical School, 1938.

IGERSHEIMER, JOSEF, c/o Mrs. Grunebaum, 462 Beacon Street, Boston.
Universities of Berlin, Strassburg and Tubingen, 1904.

KASPARIAN, KARL DER, Boston City Hospital, Boston.
Tufts College Medical School, 1935.

LICHTER, GERALD I., Boston City Hospital, Boston.
Vanderbilt University School of Medicine, 1936.

MCDONALD, EUGENE J., Boston City Hospital, Boston.
Tufts College Medical School, 1937.

MILLER, CARROLL C., 131 Park Drive, Boston.
Harvard Medical School, 1935.

MOLLIVER, HENRY, 258 Washington Avenue, Chelsea.
Middlesex University School of Medicine, 1934.

MORTARA, FRANCO, 65 Hancock Street, Boston.
University of Bologna, 1932.

PAVENSTEDT, ELEANOR, 273 Beacon Street, Boston.
University of Geneva, 1929.

ROBERTS, CHARLES P., 20 Union Park, Boston.
Emory University School of Medicine, 1935.

RUBIN, HAROLD W., 42 Nichols Street, Chelsea.
Tufts College Medical School, 1937.

SWEETSER, PETER W., Boston City Hospital, Boston.
Georgetown University School of Medicine, 1937.

WAGNER, RICHARD, 370 Commonwealth Avenue, Boston.
University of Vienna, 1912.

WHITELAW, GEORGE P., 2 Primus Avenue, Boston.
Harvard Medical School, 1935.

Milton Henry Clifford, *Secretary.*

WORCESTER DISTRICT

BACHRACH, SAMUEL, 6 Moore Avenue, Worcester.
Tufts College Medical School, 1938.

BLACKMAN, NATHAN, Worcester State Hospital, Worcester.
University of Paris, 1936.

DEE, JOHN E., Worcester City Hospital, Worcester.
Harvard Medical School, 1938.

GOLICKMAN, LOUIS, 99 Church Street, Whitinsville.
Middlesex University School of Medicine, 1933.

HARRINGTON, PHILIP V., Worcester City Hospital, Worcester.
Harvard Medical School, 1938.

HIGGINS, RAYMOND F., 39 William Street, Worcester.
McGill University Faculty of Medicine, 1937.

HORNE, ELWOOD O., 24 Holman Street, Shrewsbury.
Tufts College Medical School, 1936.

KANT, OTTO, 10 Bruce Avenue, Shrewsbury.
University of Göttingen, 1924.

LANKENNER, PETER A., 522 Grafton Street, Worcester.
Middlesex University School of Medicine, 1933.

MACDONALD, WILFRED D., Belmont Hospital, Worcester.
Tufts College Medical School, 1938.

MEYERSOHN, FRANZ, 753 Pleasant Street, Worcester.
University of Berlin, 1915.

POTTS, WILLIAM L., Worcester County Sanatorium, Worcester.
Western Reserve University School of Medicine, 1933.

ROSENBLUM, HARRY A., Brimfield Road, Fiskdale.
Kansas City University of Physicians and Surgeons, 1932.

SALOMON, ROBERT, 138 Elm Street, Worcester.
University of Frankfort, 1926.

SMITH, EUGENE F., 6 Park Terrace, Milford.
Tufts College Medical School, 1935.

STEVENS, HERMAN D., Worcester County Sanatorium, Worcester.
Jefferson Medical College of Philadelphia, 1938.

TELL, ABRAM B., 135 Chandler Street, Worcester.
Kansas City University of Physicians and Surgeons, 1931.

George C. Tully, *Secretary.*

WORCESTER NORTH DISTRICT

GROSSMAN, MYER J., 599 Main Street, Athol.
Middlesex University School of Medicine, 1933.

VERSTANDIG, CHARLES C., Fort Devens.
University of Tennessee College of Medicine, 1939.

Edward A. Adams, *Secretary.*

NEW HAMPSHIRE MEDICAL SOCIETY

DEATH

SHELDON — HAROLD E. SHELDON, M.D., of Troy, died at his home on September 24, at the age of forty.

Dr. Sheldon was born on October 24, 1899, in West Brattleboro, Vermont, a son of John E. and Cora (Brown) Sheldon. He received his degree from Boston University School of Medicine in 1936. Dr. Sheldon was a fellow of the American Medical Association.

He is survived by his widow and two brothers, Elmer H., of Lyme, and Harley F., of Hinsdale.

VERMONT STATE MEDICAL SOCIETY

VERMONT NEWS

BURLINGTON FREE DISPENSARY

The Burlington Free Dispensary will offer more coordinated and more convenient service to its patients, drawn from the underprivileged of Burlington, when it opens for 1940–41 under the management of its new full-time medical director, Dr. Theodore H. Harwood, who is also assistant professor of medicine in the University of Vermont College of Medicine. Dr. Harwood will be the first to manage the dispensary under a full-time arrangement. Under his direction, each new patient will pass through the Admissions Clinic for diagnosis before being referred to other clinics for treatment.

The times set for clinics are earlier, in order that patients may be given more prompt attention. Dr. Harwood, in addition to overseeing the whole program of clinics, will have direct supervision of the Medical Clinic, which will be held every afternoon at 2 p.m.

The Burlington Free Dispensary is operated by the City of Burlington through the Charities Department and by the University of Vermont College of Medicine. Its schedule of clinics includes surgery, medicine, pediatrics, gynecology, obstetrics, mental hygiene (for children up to eighteen), orthopedics surgery, urology, dermatology, allergy, physiotherapy, eye, ear, nose and throat, and syphilology. There is a State-operated clinic for chest diseases, and the new Squint Clinic, for the correction of cross eyes.

MISCELLANY

HARVARD UNIVERSITY MONOGRAPHS IN MEDICINE AND PUBLIC HEALTH

With the purpose of encouraging the publication of books and monographs of scientific importance by members of the Harvard Medical School and the Harvard School of Public Health, and of adding to the distinction both of the two schools and of the Harvard University Press by publishing under their auspices a noteworthy series of monographs in medicine and public health, a sum of money has been provided, to be used for an experimental period of three years, as a revolving publication fund. An editorial committee has been appointed to administer this fund, and to select books and monographs to be included in a series entitled *Harvard University Monographs in Medicine and Public Health.*

The members of the committee are Dr. A. Baird Hastings, chairman, Dr. Walter B. Cannon, Dr. J. H. Means, Dr. S. Burt Wolbach and Dr. Katherine R. Drinker, executive secretary.

Members of the faculties of the medical school and of the school of public health who have written, or who contemplate writing, books or monographs suitable for such a series have been invited to consult with the Editorial Committee and to submit their manuscripts for inclusion in the series. If financial assistance for publication of a book is required, the committee is authorized, after arrangement with the Harvard University Press, to use the publication fund for this purpose.

In order to further the economical manufacture and the successful sale of books in the monograph series, the Editorial Committee is prepared to supply to authors — via its executive secretary — consulting advice on the proper preparation of manuscripts for publication, and to make sure that announcements of books published under its auspices are widely circulated to especially interested groups.

Number 1 of the series — to be published in November — will be *The Endocrine Function of Iodine* by Dr. William T. Salter.

A. M. A. RADIO PROGRAM

"Doctors at Work" is the title of the sixth annual series of dramatized radio programs to be presented by the American Medical Association and the National Broadcasting Company.

The series will open Wednesday, November 13, and will run for thirty consecutive weeks, closing with a broadcast from the meeting of the American Medical Association at Cleveland, on June 3, 1941. The program is scheduled for 10:30 p.m. Eastern standard time (9:30 Central; 8:30 Mountain; 7:30 Pacific) over the Blue Network and other stations of the National Broadcasting Company and Canadian stations.

The programs will dramatize what modern medicine offers the individual in the way of opportunities for better health and the more successful treatment of disease. Incidental to this main theme, the programs will explain the characteristics of the different fields of modern medicine and its specialties.

Descriptive posters for local distribution may be had gratis from the Bureau of Health Education, American Medical Association, 535 North Dearborn Street, Chicago. Program titles will be announced weekly in the *Journal of the American Medical Association* and monthly in the *New England Journal of Medicine.*

NOTES

The Massachusetts Society for Mental Hygiene announces a new bulletin, *The Mental Health Sentinel,* the first number of which is being published late in October. This new magazine, which supersedes the society's monthly bulletin, is a quarterly of 24 pages and is aimed to interest all groups in the community; it will contain special articles of interest to physicians. The subscription price is $1.00 per year (four issues).

The University of California has recently announced that Dr. Walter B. Cannon, George Higginson Professor of Physiology at the Harvard Medical School, will be Charles M. and Martha Hitchcock Professor during February, 1941.

Three National Scholarships, the outstanding awards to students entering the Harvard Medical School this fall, were recently announced by Harvard University. The recipients are James S. Clarke, of La Grange, Illinois, S.B. Harvard '40; Martin E. Flipse, of Douglaston, Long Island, New York, A.B. Hope College '40; and Winsor C. Schmidt, of Rye, New York, who attended Yale. This is the fourth year of the medical school's National Scholarship plan, which is similar to that introduced in Harvard College in 1934, and subsequently adopted by

the Graduate School of Arts and Sciences and the Graduate School of Design. Winners of the scholarships who maintain honor records continue to hold the awards until graduation.

NOTICES

BOSTON DOCTORS' SYMPHONY ORCHESTRA

The Boston Doctors' Symphony Orchestra will rehearse under Alexander Thiede, former concertmaster with the Cleveland Symphony Orchestra, every Thursday at 8:30 p.m. Those interested in becoming members should communicate with Dr. Julius Loman, Pelham Hall Hotel, Brookline (BEA 2430).

PETER BENT BRIGHAM HOSPITAL

A joint medical and surgical clinic at the Peter Bent Brigham Hospital will be held on Wednesday, October 30, from 2 to 4 p.m. Drs. E. C. Cutler and Soma Weiss will speak, their subject being "The Unconscious Patient." A clinicopathological conference, conducted by Dr. Elliott C. Cutler, will take place from 4 to 5 p.m.

Physicians and students are cordially invited to attend.

MASSACHUSETTS GENERAL HOSPITAL

A meeting of the Hospital Research Council will be held in the Ether Dome of the Massachusetts General Hospital on Tuesday, October 29, at 5:00 p.m.

PROGRAM

Studies Pertaining to the Physiologic and Therapeutic Effects of Low Temperature:

Clinical Aspects and Renal Function. Dr. John H. Talbott.

Constituents of Blood and Respiratory Functions. Drs. D. Bruce Dill and William H. Forbes.

Therapeutic Considerations in Schizophrenia. Dr. Kenneth J. Tillotson.

JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston
Lecture Hall, 9–10 a.m.

MEDICAL CONFERENCE PROGRAM, NOVEMBER–DECEMBER

Friday, November 1 — Lupus Erythematosus: Case report and pathological discussion. Dr. H. E. MacMahon.

Saturday, November 2 — Hospital Case Presentation. Dr. S. J. Thannhauser.

Tuesday, November 5 — Management of Pulmonary Abscess. Dr. R. H. Betts.

Wednesday, November 6 — Hospital Case Presentation. Dr. S. J. Thannhauser.

Thursday, November 7 — Carcinoma of the Pancreas: Clinical review of cases. Dr. E. P. Engleman.

Friday, November 8 — Experimental Studies in Pernicious Anemia. Dr. M. M. Wintrobe.

Saturday, November 9 — Hospital Case Presentation. Dr. S. J. Thannhauser.

Tuesday, November 12 — Narcolepsy: A review and presentation of cases. Dr. W. F. Murphy.

Wednesday, November 13 — Hospital Case Presentation. Dr. S. J. Thannhauser.

Thursday, November 14 — Motion Picture: Ovulation and Effects of Pregnant Mares' Serum — Gonadogen.

Friday, November 15 — Ménière's Disease. Dr. Donald Munro.

Saturday, November 16 — Hospital Case Presentation. Dr. S. J. Thannhauser.

Tuesday, November 19 — The Present Status of Urinary Tract Calculi. Dr. H. W. Sulkowitch.

Wednesday, November 20 — Hospital Case Presentation. Dr. S. J. Thannhauser.

Thursday, November 21 — Dysmenorrhea. Dr. L. E. Phaneuf.

Friday, November 22 — The Formation of Biliary Calculi. Dr. L. Lichtwitz.

Saturday, November 23 — Hospital Case Presentation. Dr. S. J. Thannhauser.

Tuesday, November 26 — X-ray Demonstration. Dr. A. Ettinger.

Wednesday, November 27 — Hospital Case Presentation. Dr. S. J. Thannhauser.

Friday, November 29 — Marble Bone Disease. Dr. Albert Frank.

Saturday, November 30 — Hospital Case Presentation. Dr. S. J. Thannhauser.

SUFFOLK DISTRICT MEDICAL SOCIETY

There will be a meeting of the Suffolk District Medical Society in the Princess Ballroom of the Hotel Somerset, 400 Commonwealth Avenue, on Wednesday, October 30.

PROGRAM

12:00 m. Luncheon, gratis to those members notifying the secretary at least twenty-four hours in advance.

12:30 p.m. Stated Meeting.

1:00 p.m. Lessons for Physicians and Surgeons from the Army and Navy. Capt. J. J. A. McMullen, M.C., U. S. N.; Col. J. J. Reddy, M.C., U. S. A.; and Lt.-Col. A. R. Bolling, G.S.C., U. S. A.

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS, UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	ORTHOPEDIC CONSULTANT
Lowell	November 1	Albert H. Brewster
Salem	November 4	Harold C. Bean
Haverhill	November 6	William T. Green
Gardner	November 12	Mark H. Rogers
Brockton	November 14	George W. Van Gorder
Worcester	November 15	John W. O'Meara
Pittsfield	November 18	Francis A. Slowick
Northampton	November 20	Garry deN. Hough, Jr.
Hyannis	November 26	Paul L. Norton
Fall River	November 27	Eugene A. McCarthy

NEW ENGLAND HEART ASSOCIATION

There will be a special meeting of the New England Heart Association at the Boston Medical Library in honor of the late Dr. Maude E. Abbott on Friday, November 8, at 8:15 p.m.

PROGRAM

In Honor of Dr. Maude E. Abbott:

Dr. Abbott and McGill University. Dr. Charles S. Martin, of Montreal.

Her Contribution to Cardiology. Dr. Paul D. White.

Personal Reminiscences. Dr. Emanuel Libman, of New York City.

Changes Which Occur During Life in Patients with Congenital Malformations of the Heart. Dr. Helen B. Taussig, of Baltimore.

Interested physicians and medical students are invited to attend.

NEW ENGLAND PEDIATRIC SOCIETY

There will be a meeting of the New England Pediatric Society on Wednesday, October 30. The clinical presentation will be held at the Cheever Amphitheater, Dowling Building, Boston City Hospital, and all the other events at Longwood Towers, Brookline.

PROGRAM

4:00 Dry Clinic: Dr. Edwin H. Place and his associates.
6:00 Refreshments.
7:00 Dinner.
8:00 "When Bobby Goes to School," a moving picture. The Prevention, Diagnosis and Treatment of Some of the Common Contagious Diseases. Dr. Philip M. Stimson, visiting physician, Willard Parker Hospital, New York City.

THOMAS WILLIAM SALMON MEMORIAL LECTURES

The Salmon Committee on Psychiatry and Mental Hygiene invites the members of the medical profession and their friends to the Eighth Series of Thomas William Salmon Memorial Lectures.

This series will be given by Dr. Nolan D. C. Lewis, director of the New York State Psychiatric Institute, and professor of psychiatry at Columbia University. The lectures will be given on successive Friday evenings, November 8, 15 and 22, at 8:30 p.m., at the New York Academy of Medicine, 2 East 103rd Street, New York City. Dr. Lewis will speak on "The Pathway of Research in Psychiatry."

UNITED STATES CIVIL SERVICE COMMISSION

The Civil Service Commission announces that enough applications have been received to meet the prospective need for temporary and part-time civilian medical officers in connection with the Army expansion.

The commission calls attention to the fact, however, that there is an urgent need for medical officers and senior and associate medical officers to fill permanent positions in other agencies. Applications will be received until further notice. The positions pay from $3200 to $4600 a year. Fourteen specialized branches of medicine are included.

There is also an urgent need to fill junior medical officer positions at $2000 a year at St. Elizabeths Hospital, Washington, D. C.

Full information and application forms for these examinations may be obtained at the office of the Secretary, Board of United States Civil Service Examiners at any first- or second-class post office, from the United States Civil Service Commission, Washington, D.C., or from any of the commission's district offices.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING SUNDAY, OCTOBER 27

MONDAY, OCTOBER 28

12:15–1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

TUESDAY, OCTOBER 29

*9–10 a.m. Food Allergy. Dr. E. A. Brown. Joseph H. Pratt Diagnostic Hospital.

12:15–1:15 p.m. Clinicoroentgenological conference. Peter Bent Brigham Hospital amphitheater.

5 p.m. Hospital Research Council. Massachusetts General Hospital.

WEDNESDAY, OCTOBER 30

*9–10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*12 m. Clinicopathological conference. Children's Hospital.

*2–4 p.m. The Unconscious Patient. Drs. E. C. Cutler and Soma Weiss. Peter Bent Brigham Hospital.

4–5 p.m. New England Pediatric Society. Boston City Hospital, Cheever amphitheater.

6–8 p.m. New England Pediatric Society. Longwood Towers, Brookline.

THURSDAY, OCTOBER 31

*8:30 a.m. Combined clinic of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital, at the Peter Bent Brigham Hospital.

*9–10 a.m. Fever Therapy in Diseases of the Nervous System. Dr. S. H. Epstein. Joseph H. Pratt Diagnostic Hospital.

FRIDAY, NOVEMBER 1

*9–10 a.m. Lupus Erythematosus: Case report and pathological discussion. Dr. H. E. MacMahon. Joseph H. Pratt Diagnostic Hospital.

SATURDAY, NOVEMBER 2

*9–10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*Open to the medical profession.

NOVEMBER 1–30 — Joseph H. Pratt Diagnostic Hospital. Page 691.

NOVEMBER 8 — New England Heart Association. Page 691.

NOVEMBER 8, 9 — Society for Research in Child Development. Page 648, issue of October 17.

NOVEMBER 8, 15 and 22 — Thomas William Salmon Memorial Lectures. Notice above.

NOVEMBER 13, 14 — New England Postgraduate Assembly. Cambridge, Massachusetts.

NOVEMBER 14 — Pentucket Association of Physicians. Page 263, issue of August 15.

NOVEMBER 14 — American Conference on Industrial Health. Page 648, issue of October 17.

NOVEMBER 15 — Massachusetts Society for Mental Hygiene. Page 648, issue of October 17.

DECEMBER 27–29 — National Convention of the Association of Medical Students, Boston.

JANUARY 4, 1941 — American Board of Obstetrics and Gynecology. Page 1064, issue of June 20.

MARCH 8 — American Board of Ophthalmology. Page 201, issue of August 1.

APRIL 21–25 — American College of Physicians. Page 1065, issue of June 20.

MAY 21, 22 — Massachusetts Medical Society, Boston.

JUNE 2–6 — American Medical Association. Cleveland, Ohio.

DISTRICT MEDICAL SOCIETIES

FRANKLIN

NOVEMBER 12.
JANUARY 14.
MARCH 11.
MAY 13.

Meetings will be held at 11 a.m. at the Franklin County Hospital, Greenfield.

NORFOLK

OCTOBER 29 — Page 648, issue of October 24.

SUFFOLK

OCTOBER 30 — Page 691.
NOVEMBER 7 — Censors' meeting. Page 305, issue of August 22.

JANUARY 29 — Page 604, issue of October 10.
APRIL 30 — Page 604, issue of October 10.

WORCESTER
NOVEMBER 13 — Grafton State Hospital, Grafton.
DECEMBER 11 — St. Vincent Hospital, Worcester.
JANUARY 8, 1941 — Worcester City Hospital, Worcester.
FEBRUARY 12 — Worcester State Hospital, Worcester.
MARCH 12 — Memorial Hospital, Worcester.
APRIL 9 — Hahnemann Hospital, Worcester.

Supper at 6:30 p.m. followed by a business meeting and scientific program.

BOOK REVIEWS

On Oxidation, Fermentation, Vitamins, Health and Disease. By Albert V. Szent-Györgyi, M.D., Ph.D., D.H.C. 12°, cloth, 109 pp. Baltimore: Williams & Wilkins Company, 1939. $2.00.

This formidable title embraces five Abraham Flexner Lectures given in 1939 at Vanderbilt University School of Medicine and published for the University. The distinguished 1937 Nobel prize winner and professor of medical chemistry at the University of Szeged, Hungary, has summarized in simple but vivid and personal language the results of his investigations on biological oxidation, pursued during the past fifteen years. It was a difficult task to present such a highly technical subject to a general medical-school audience, but Dr. Szent-Györgyi has done it in a fruitful and inspiring way, and with the brevity of about a hundred printed pages.

The first lecture deals with the problem of biological oxidation — the long series of controlled chemical reactions whereby carbohydrates are oxidized, through the agency of the animal's specific enzymes, so gradually that at every stage the animal cell can utilize the small quantity of energy liberated.

Muscle respiration is the subject of the second lecture. Here another similar chain of oxidations is traced, each reaction being made possible by a specific enzyme or catalyst of the animal cell.

The third lecture concerns fermentation and its relation to oxidation. Fermentation is essentially an anerobic molecular rearrangement with the liberation of quantities of energy much smaller than those concerned in oxidation, but still sufficient to support life in the form of bacteria and yeasts, and of use in muscular activity in man. One of the reactions involved in muscle fermentation is decarboxylation. Curiously, the coenzyme decarboxylase, concerned in this reaction, is found to be identical with phosphorylated vitamin B_1. Thus vitamin B_1 deficiency becomes explicable in terms of interference with the normal decarboxylation in muscle.

In the fourth lecture, on vegetation oxidations, the author mentions his discovery of a substance concerned with plant oxidation systems, which later proved to be ascorbic acid. Szent-Györgyi thus became the father of vitamin C.

The concluding lecture, on vitamins, health and disease, begins by asking why man cannot synthesize in his body the substances we call vitamins. Some of them can be made by other animals, notably vitamin C by the rabbit, and it is suggested that our long tropical ancestry, with its continuous supply of green plants, has lost us the ability to make this substance.

In expounding his "general theory of health and disease," Szent-Györgyi unfortunately goes off the deep end. He paints a picture of man in his natural jungle environment, perfectly adapted to it and therefore perfectly healthy. As a more modern counterpart he cites the island of Tristan da Cunha, "where man of our own race lives a natural life and knows no disease." Again, he states: "Tuberculous patients are sent to the mountains and it is known that no tuberculosis exists above 9000 feet. . . . [The mountain air] is simply the air we are made for, and if we have what we are made for there will be no tuberculosis." In other words, practically all disease is merely maladjustment to the present environment.

On the whole this is a very stimulating and valuable little volume, heartily to be recommended.

Let's Talk About Your Baby. By H. Kent Tenney, Jr., M.D., with a foreword by Joseph Brennemann, M.D. Second edition. 12°, cloth, 115 pp., with 13 illustrations. Minneapolis: University of Minnesota Press, 1940. $1.00.

Books dealing with the problems of the baby's first year are relatively numerous and for the most part sound, but from the standpoint of reading, most of them have little appeal. This one, however, aims to be enjoyable as well as instructive; and this end has been surprisingly well achieved. Information regarding "food, furniture, clothing, habits, parents, doctors and diseases" is presented with a most welcome freedom from dogmatism and rigidity. It should be helpful to a young mother in many ways, not the least of which will be to relieve the notion that in bringing up her young one she will have to learn and conform to a regime as inflexible as the edicts of Media and Persia. This book is highly recommended.

Your Marriage: A guide to happiness. By Norman E. Himes, S.B., A.M., Ph.D. 8°, cloth, 434 pp., with 12 charts. New York: Farrar and Rinehart, 1940. $3.75.

The author has succeeded in living up to the claims of the omnibus on the book jacket by making available a discussion of the psychological, the physical and the economic aspects of marriage.

Directed with greatest effectiveness at the educated and unattached young person, this book offers an objective and factual approach to happiness in marriage. It is completely documented, and never fails to differentiate fact and opinion. The reprinting of the actual tests to predict marital happiness and adjustment, with instructions for self-scoring, forms an important part of the book. The author bases much of his material on the results of these tests. Therefore the reader should be constantly aware of the author's point of view; that is, "Unfortunately, some of the newer scientific results run counter to not a few of the widely accepted opinions of authorities. Wherever there has been a conflict . . . between revolutionary principles statistically determined on a small sample . . . and the judgment and conclusions of experts based upon their wide knowledge of human nature, history, clinical experience and science in general, I have accepted the latter. . . . Until such time . . . as there are corroboratory studies on marriage besides those by Professor Terman and by Professors Burgess and Cottrell, I think we should view such studies with sympathy but caution" (page 10).

While it offers nothing new on sex life in marriage, sexual adjustment and the art of love, to which two chapters are devoted, the book does include an excellent bibliography on "sexual enlightenment," and weighs the advantages of reading as opposed to personal counseling in specific situations. Equally valuable is the listing of counseling centers.

The approach to the advantages of early marriage is put forth satisfyingly and realistically, and the chances

of its success are probably enhanced by a consideration of the factors of background and personality. Perhaps the most unique and valuable contribution is the discussion of finances, budget, credit, insurance, housing and the general job of being a consumer. Added to this is the fact that such subjects are ably discussed along with the more usual chapters on emotional and physical adjustment. To the normal young person whose goal is marriage and whose education has fitted him or her to prepare for it at least as painstakingly as for any other situation, the book may indeed be "a guide to happiness."

Fractures and Other Bone and Joint Injuries. By R. Watson-Jones, M.Ch., B.Sc., Ch.B., M.B., M.R.C.S. (Eng.). 8°, cloth, 723 pp., with 1040 illustrations. Baltimore: Williams & Wilkins Co., 1940. $13.50.

This book includes orthopedic practices which have been developed in many parts of the world. The author's breadth of vision and experience can best be understood by reading the first chapters on the physiology and pathology of osseous tissues. A mastery of these principles enables one to establish a set of criteria to evaluate new methods. With this background the author has searched widely and assembled much of the best thought on orthopedic problems.

The necessity for complete immobilization of fractures is continually stressed; but the author also emphasizes the dangers of overimmobilization and the attendant morbidity caused by unnecessary stiffness in joints. The exactness of his descriptions in the treatment of individual fractures and joint diseases enables one to follow his methods closely. There is a timely chapter on the omnipresent backache and the importance of prolapsed intervertebral disks in chronic sciatica. The Winnett–Orr treatment of compound fractures and the aftercare following the original cast are described in detail.

There are a great number of excellent x-ray pictures and diagrams for the illustration of the text. Another feature of the book is a comprehensive and up-to-date bibliography.

It was the English school of surgeons who gave the greatest impetus to orthopedic surgery during World War I, and this book shows how well they have continued their leadership in this field during peacetime.

The Journal of Gideon Mantell, Surgeon and Geologist, Covering the Years 1818–1852. Edited, with an introduction and notes, by E. Cecil Curwen. 8°, paper, 293 pp. London: Oxford University Press, 1939. $4.25.

Dr. Mantell was a surgeon and general practitioner who lived in Lewes, England, and kept a diary from 1818 to 1852. In addition to his practice, he carried on extensive investigations concerning the geology of the district about Lewes, which culminated in a book, *The Fossils of the South Downs,* published in 1822. He frequently traveled to London at the time when he was intimate with Sir Charles Lyell, Thomas Hodgkin and others. There are excellent descriptions of the early meetings of the British Association for the Advancement of Science. Through the efforts of his friend, Professor Silliman, he received the degree of LL.D. from Yale University in 1834. Dr. Morton, of Philadelphia, dedicated a geological work to him. Dr. Mantell's geological collection was sold to the British Museum. In medicine, he contributed frequent papers to the *Lancet.* After leaving Lewes, he practiced for many years in Clapham, and became a member of the Royal Society. His journal reflects the medical and scientific life of England one hundred years ago, as recorded by a physician, who, in addition to his practice of medicine, was a scientist of note. This is an important historical document, carefully edited.

Cancer in Childhood. By Harold W. Dargeon, M.D. 4°, cloth, 114 pp., with 42 illustrations and 6 tables. St. Louis: C. V. Mosby Company, 1940. $3.00.

This book represents the communications of eleven authors, and it aims to cover not merely cancer proper but all the malignant tumors which may occur in the early years of life. The observations were made at the Memorial Hospital for the Treatment of Cancer and Allied Diseases in New York City, with the purpose of correcting the rather general impression that cancer in youth is a matter of no very great importance because of its rarity. The greatest number of facts and conclusions that can now be assembled are collected and published in this book; they should be of interest to all who care medically for the young. There is nothing of finality in the presentation, nor is there intended to be, only the hope of awakening interest in further study.

An Introduction to Medical Genetics. By J. A. Fraser Roberts, M.A., M.B., D.Sc., F.R.S.E. 8°, cloth, 266 pp., with 94 illustrations. London: Oxford University Press, 1940. $4.50.

Practitioners of medicine rarely have the inclination to study a book on mammalian genetics. For such gentlemen, Dr. Roberts offers the structural framework on human genetics. The subject is addressed to the senior student and to the clinician; it deals with the human subject as observed in the community, in medical practice and in the hospital. Some of the entities considered are: brachydactyly, alkaptonuria, Osler's disease (multiple telangiectasia), night blindness, Huntington's chorea, albinism, hemophilia, blood groups and so forth. There is an excellent chapter on heredity as a factor in the causation of disease. The book closes with notes on the recording of genetic data.

It seems to the reviewer that this is a timely book, since increased emphasis is being placed on hereditary constitution as one of the factors to be considered in discussions on the causation of disease, as presented by teachers in medical schools and in hospitals.

An Anatomical Analysis of Sports. By Gertrude Hawley, M.A. 8°, cloth, 191 pp., with 97 illustrations. New York: A. S. Barnes & Company, 1940. $3.00.

This is another Barnes book written primarily for physical educationists and coaches. The careful description of muscular action and joint function is well done, and although one cannot entirely agree with everything the author writes, on the whole it is a careful analytical study. One who is not a physical educationist could definitely take issue with the author in some of her descriptions, listings and classifications of muscle groups with definite functional action.

Admirable analytical descriptive material, well correlated, is presented for the individual sports discussed, namely, archery, baseball, basketball, horseback riding, fencing, field hockey, football, golf, swimming and diving, tennis and track, field and winter sports. This is interesting to all those who are concerned in the detail of this material.